



XIX CONGRESSO
NAZIONALE
SIES 2026

**LO STUDIO DEL RUOLO E DELL'ORIGINE CELLULARE
DELLE VESICOLE EXTRACELLULARI COME
BIOMARCATORI NELLA TERAPIA CART**

Giuseppe LIA

Department of Molecular Biotechnology and Health Sciences University of Torino, Italy

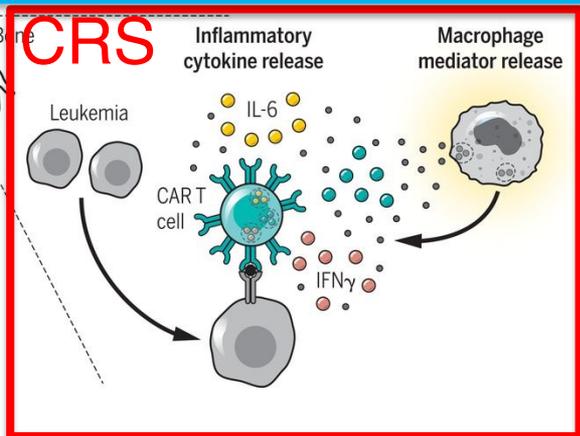
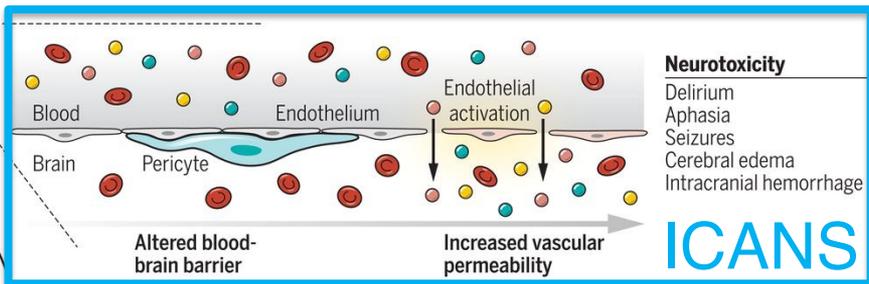
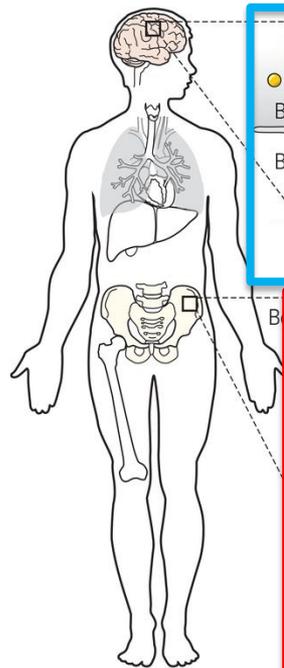
Firenze | 4-6 marzo 2026
Palazzo degli Affari



Disclosures of Name Surname

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
nothing to declare							

Toxicities of CAR T-cells Therapy



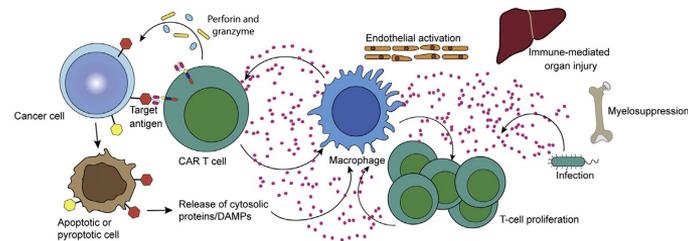
Hemodynamic instability

- Tachycardia
- Hypotension
- Capillary leak syndrome

Organ dysfunction

- AST and ALT elevation
- Hyperbilirubinemia
- Respiratory failure

Immune effector cell-associated haematotoxicity



ICAHT

Local inflammation in bone marrow
 Genotoxicity from prior therapies
 Systemic inflammatory mediators

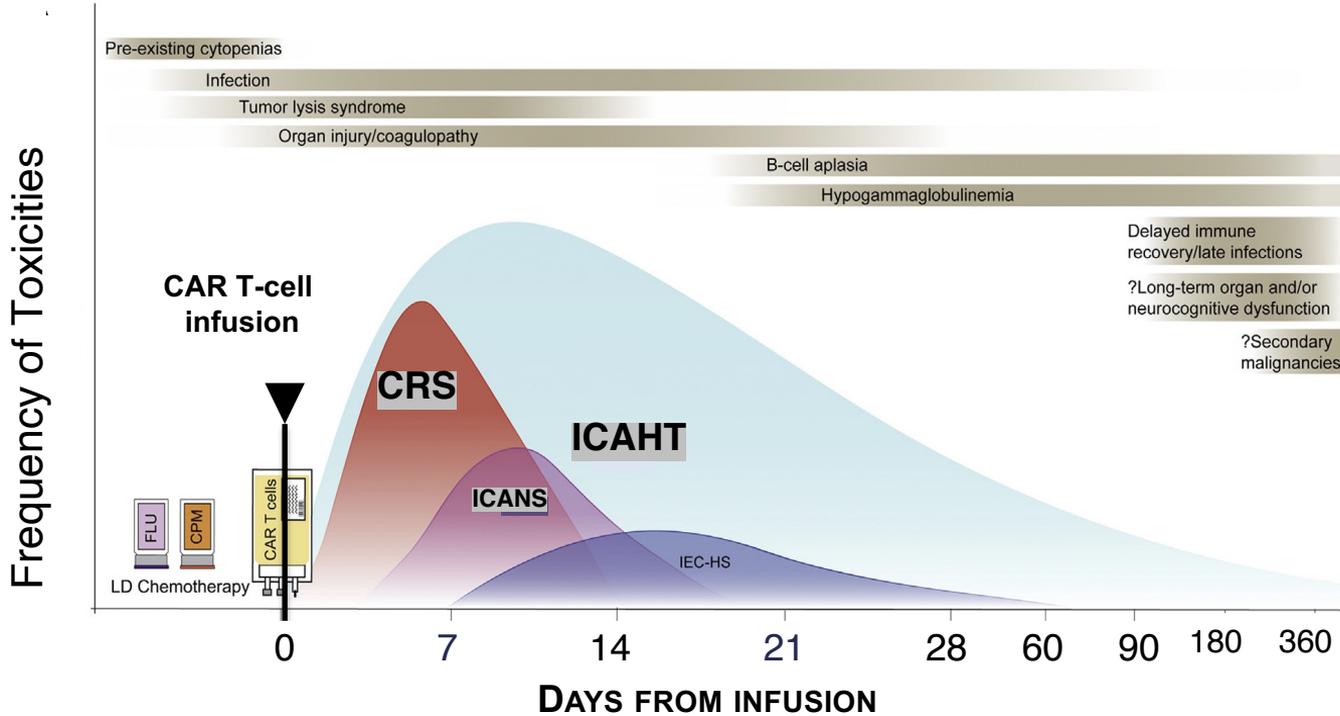


myelosuppression

Immune effector cell-associated haematotoxicity after CAR T-cell therapy: from mechanism to management Kai Rejeski, Michael D Jain, Nirali N Shah, Miguel-Angel Perales, Marion Subklewe, *Lancet Haematol* 2024; 11: e459–70
 INSPIRED Symposium Part 3: Prevention and Management of Pediatric Chimeric Antigen Receptor T Cell-Associated Emergent Toxicities. Kevin O. McNerney et al. *Transplantation and Cellular Therapy* 30 (2024) 38–55.

ALT, alanine aminotransferase; AST, aspartate aminotransferase; CAR T, chimeric antigen receptor T cell; CRS, cytokine release syndrome; IFN, interferon; IL, interleukin.
 June CH, O'Connor RS, Kawalekar OU, Ghassemi S, Milone MC. *Science*. 2018;359(6382):1361-1365.

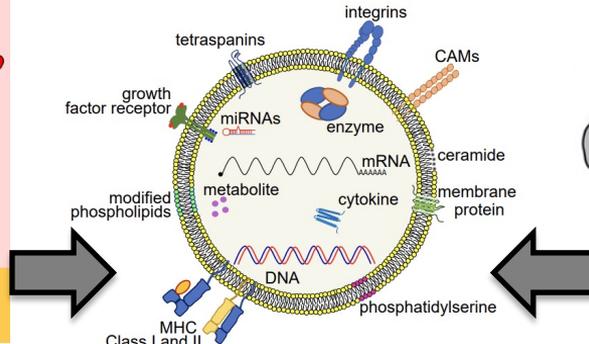
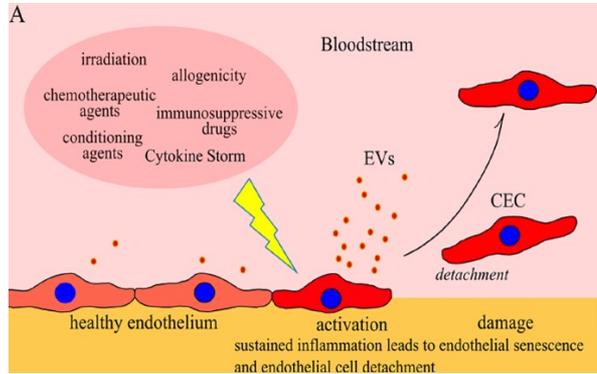
Typical Onset and Resolution of CRS & Neurologic Events



Lee DW, Gardner R, Porter DL, et al. *Blood*. 2014;124(2):188-195.
 Maus MV, et al. *Journal for ImmunoTherapy of Cancer*. 2020;8:e001511.
 Kevin O. McNerney et al. *Transplantation and Cellular Therapy* 30 (2024) 38 55.

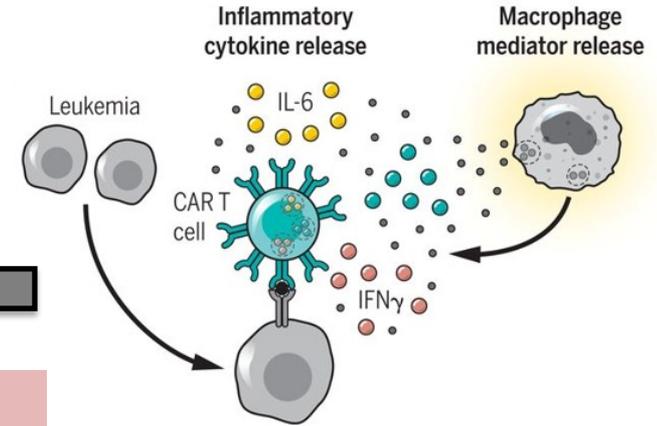
Endothelial damage and Leukocyte activation as EVs source

Endothelial Cells



increase production of extracellular vesicles

Leukocytes



Biomarkers for Early Complications of Endothelial Origin After Allogeneic Hematopoietic Stem Cell Transplantation: Do They Have a Potential Clinical Role?
Giuseppe Lia, Luisa Giaccone, Sarah Leone and Benedetto Bruno (2021) *Front. Immunol.* 12:641427.



Multiparametric Flow-Cytometry on individual EVs (absolute count of EVs originated from Endothelial cells, Leukocytes and Platelet)

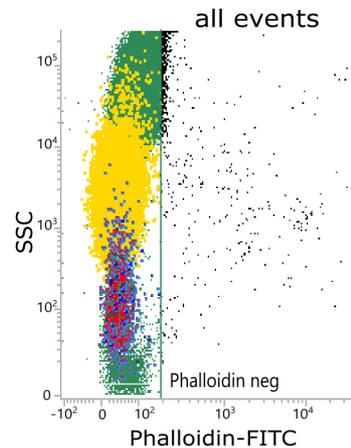


antibodies panel

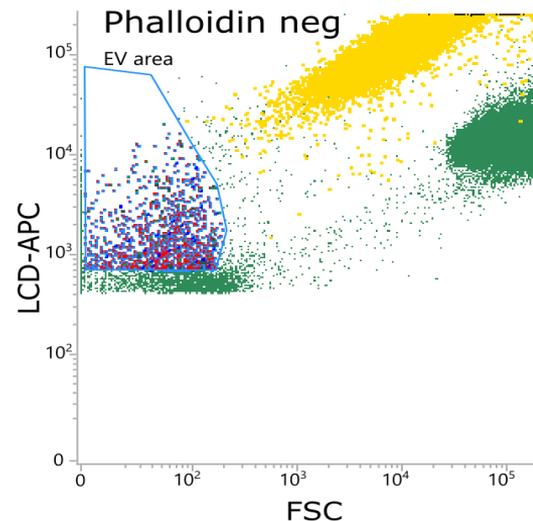
- Phalloidin-FITC
- LCD-APC
- CD41a-PE
- CD31-PE-Cy7
- CD45-V500
- CD146-BV786



Unbroken particle



EVs



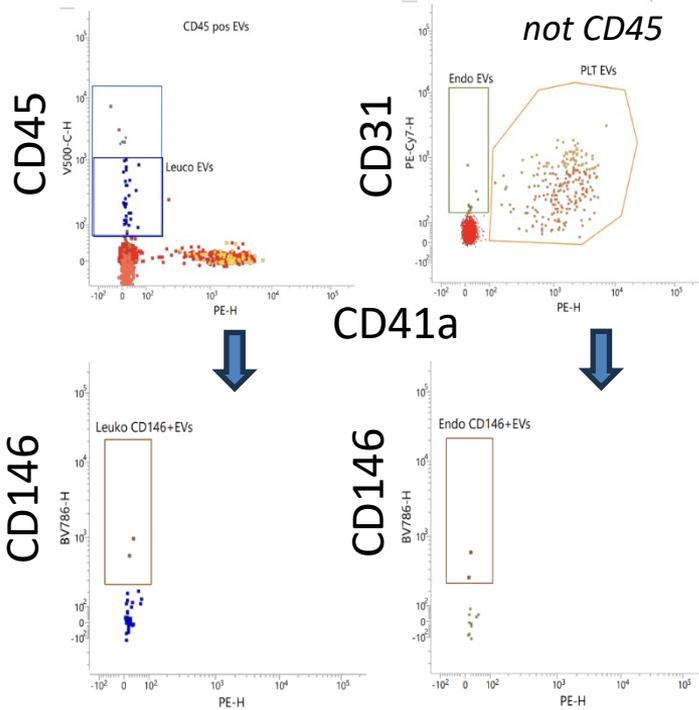
Marchisio M. et al. (2020) International Journal of Molecular Sciences 22(1):48
DOI:10.3390/ijms22010048



Multiparametric Flow-Cytometry on individual EVs (absolute count of EVs originated from Endothelial cells, Leukocytes and Platelet)

Leuko EVs

Endo and PLT EVs



Consecutive enrollment of patients who undergo CAR T-cells therapy

EDTA samples collected at pre-lymphodepletion, on infusion day and at days:

+1,+3,+7,+10,+14,+20-30



Patients Characteristic

Patients	33
Median age, years (range)	64 (range 39-75)
Male	18 (54.5%)
Diagnosis, n (%)	
Diffuse Large B-cell Lymphoma (DLBCL)	21 (63.6%)
Follicular Lymphoma (FL)	7 (21.2%)
Mantle Cell Lymphoma (MCL)	3 (16.7%)
Multiple Myeloma	2 (6.1%)
CAR-T Product, n (%)	
Axicabtagene ciloleucel (Axi-cel)	21 (63.6%)
Tisagenlecleucel (Tisa-cel)	7 (21.2%)
Brexucabtagene autoleucel (Brexu-cel)	3 (9.1%)
Idecabtagene vicleucel (Ide-cel)	2 (9.1%)
Toxicities treatment, n (%)	
Anti-cytokine therapy (Tocilizumab)	28 (84.8%)
Steroids	23 (69.7%)
Other	2 (6.1%)
Disease Status at Infusion, n (%)	
Progressive Disease (PD)	27 (81.8%)
Partial Remission (PR)	3 (9.1%)
Complete Remission (CR)	1 (3.03%)
Stable Disease (SD)	1 (3.03%)
Very Good Partial Remission (VGPR)	1 (3.03%)
Post-CART Toxicities, n (%)	
CRS (Any Grade)	28 (84.8%)
Median onset, days (range)	2.5 (range 0-8)
Grade 1	22
Grade 2	6
ICANS (Any Grade)	9 (27.3%)
Median onset, days (range)	6 (range 3-19)
Grade 1	7
Grade 2	2
Prolonged Cytopenia (lasting > Day 30)	16 (48.5%)
Prolonged Thrombocytopenia (lasting > 21 days)	15 (45.5%)
Prolonged Neutropenia (lasting > 21 days)	7 (21.2%)
Infectious Complications	6 (18.2%)

Post-CART Toxicities, n (%)

CRS (Any Grade)

Median onset, days (range)

Grade 1

Grade 2

28 (84.8%)

2.5 (range 0-8)

22

6

ICANS (Any Grade)

Median onset, days (range)

Grade 1

Grade 2

9 (27.3%)

6 (range 3-19)

7

2

Prolonged Cytopenia (lasting > Day 30)

Prolonged Thrombocytopenia (lasting > 21 days)

Prolonged Neutropenia (lasting > 21 days)

Infectious Complications

16 (48.5%)

15 (45.5%)

7 (21.2%)

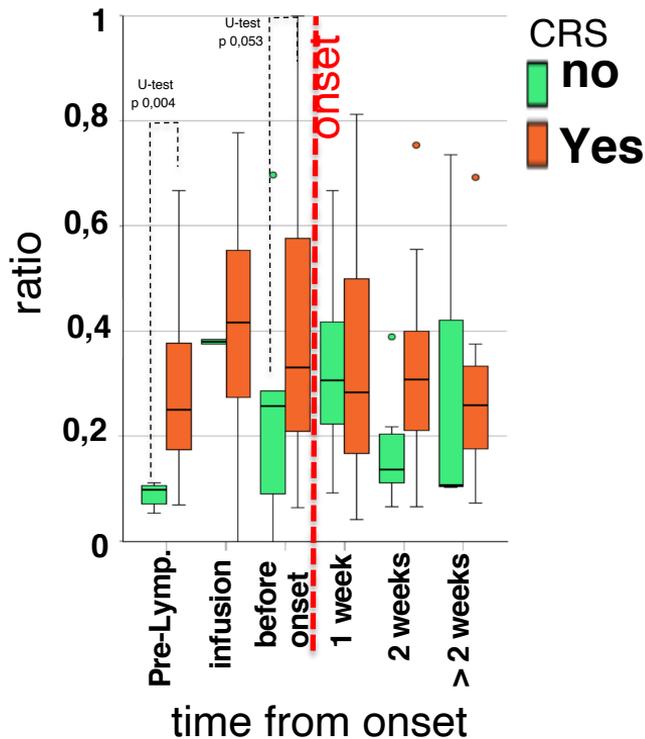
6 (18.2%)



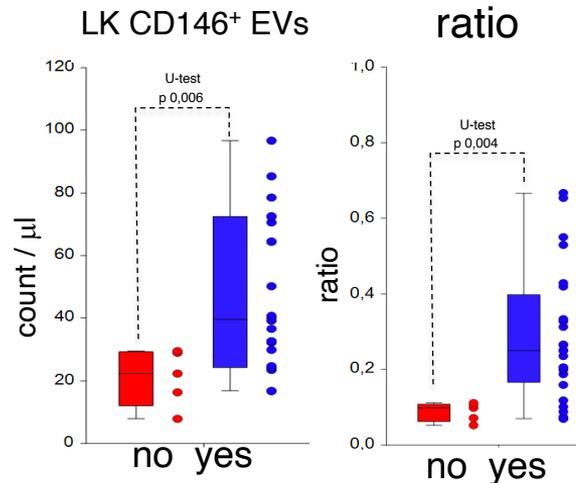
EVs subtypes dynamics after CAR T-cell infusion

CRS

LK CD146⁺ EVs / LK EVs



pre-lymphodepletion



Logistic regression

OR 1,14
p-value 0,022

AUROC
0,871 (ci: 0,721-1)

Logistic regression

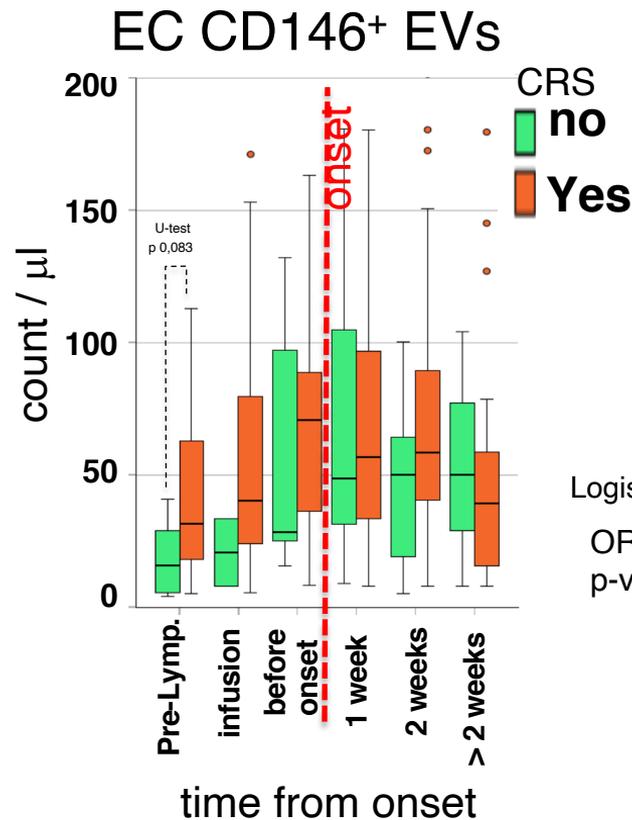
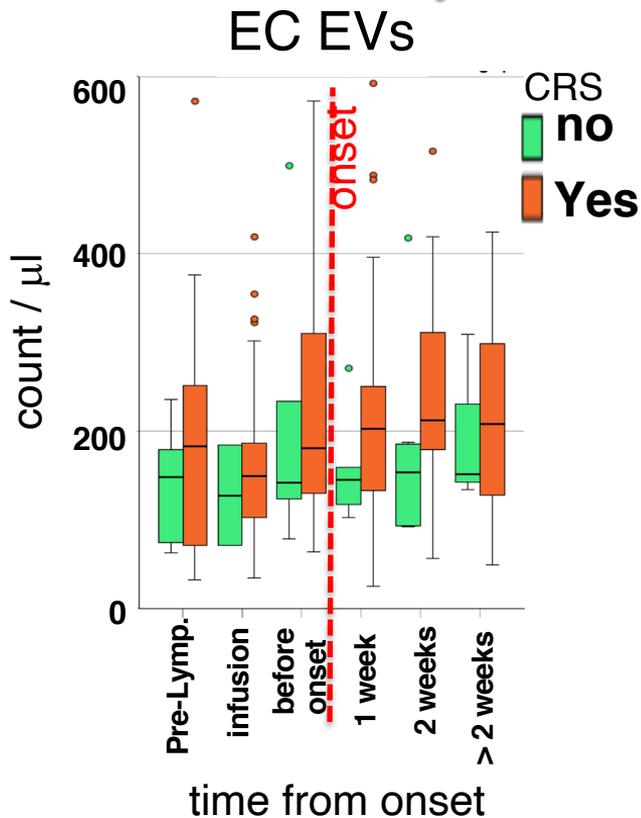
OR >100
p-value <0,001

AUROC
0,886 (ci: 0,769-1)



EVs subtypes dynamics after CAR T-cell infusion

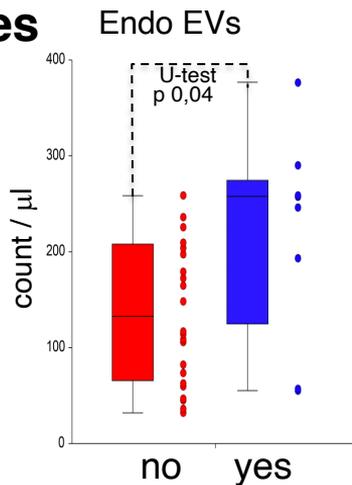
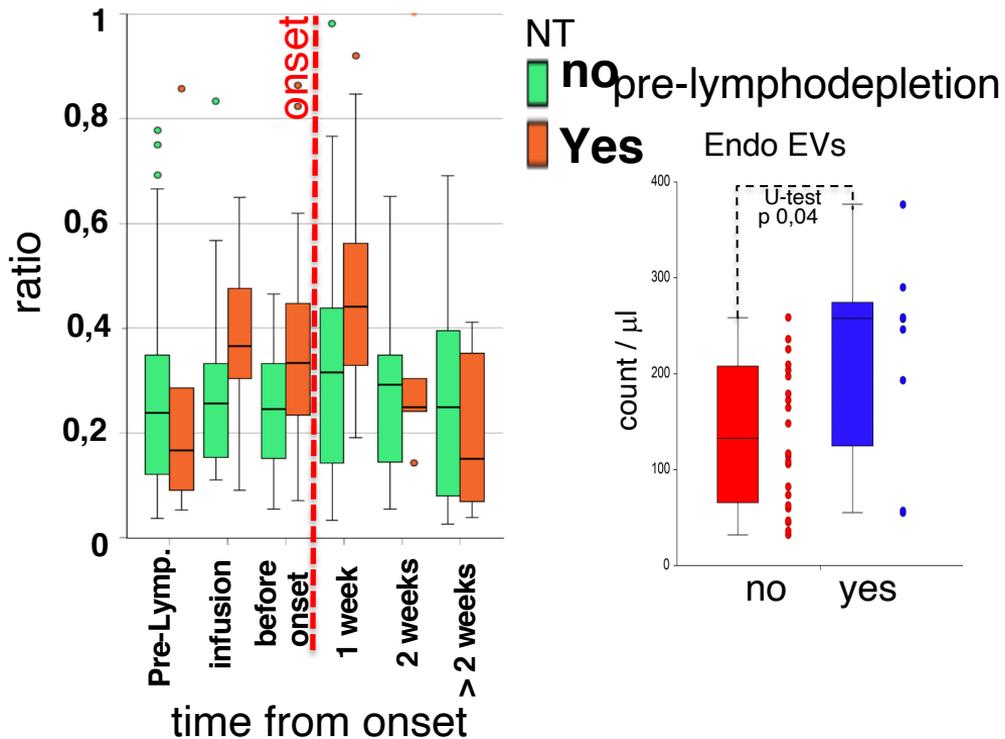
CRS



EVs subtypes dynamics after CAR T-cell infusion

ICANS

EC CD146+ EVs / EC EVs

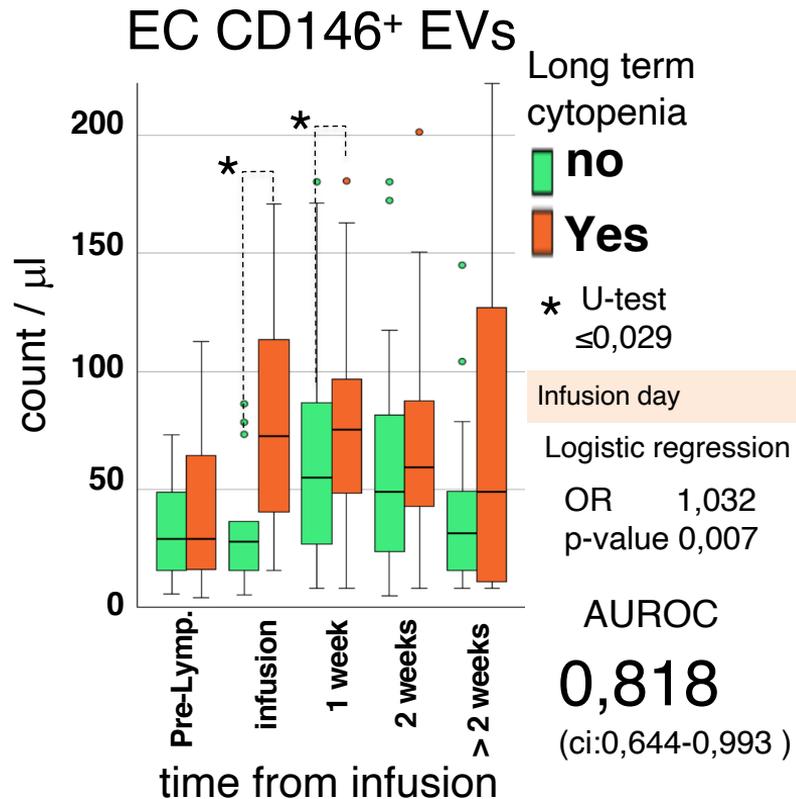
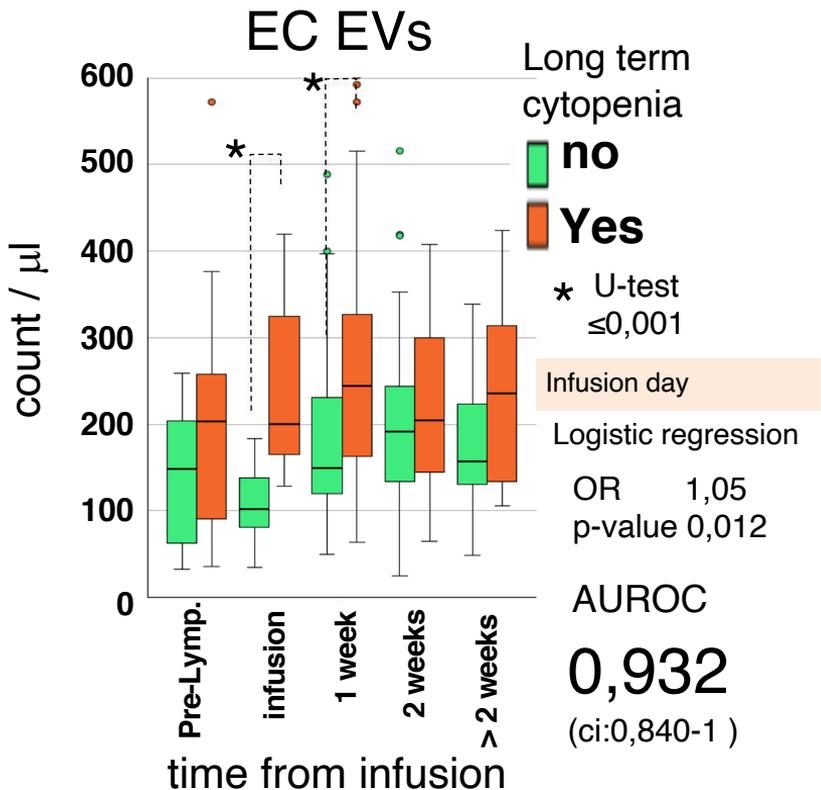


Before onset
 Increase of
 EC CD146+
 Count EVs

Logistic regression
 OR 1,01
 p-value 0,075

EVs subtypes dynamics after CAR T-cell infusion

cytopenia



Conclusions and Next Steps

Despite limited patient size of the study

The study showed peculiar dynamics of different EVs subtypes before CART toxicities

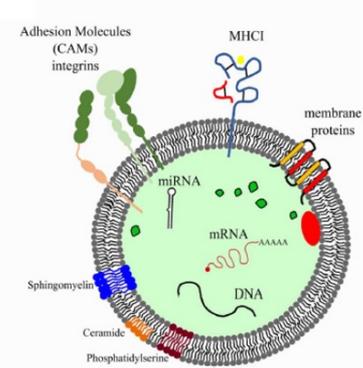
EVs originated from activated Leukocytes are the most correlated with CRS

Evs originated from activated Endothelial cell are the most correlated with NT
And with cytopenia

- Potential diagnostic and prognostic values remain to be determined

In progress:

- We are evaluating other cell markers **Circulant Endothelial Cells** and **Endothelial Progenitor Cells**
- We are other biomarkers using multiplexed assay



Acknowledgments

Emat. Universitaria

Benedetto Bruno
Luisa Giaccone
Irene Dogliotti
Federica Ferrando
Michele Dicataldo
Alessia Melis
Simone Ragaini,
Michele Clerico,
Federica Cavallo
Mattia Novo



EMAT. Ospedal

Alessandro Busca
Chiara Maria DellaCasa
Valentino Granero
Barbara Botto

CPO Centro Epidemiologia Oncologica/Epidemiologia Clinica, Torino, Italy:

A. Evangelista



Thank you for your attention !

