

# **New Agents in DLBCL – Targeting** **Macrophages**

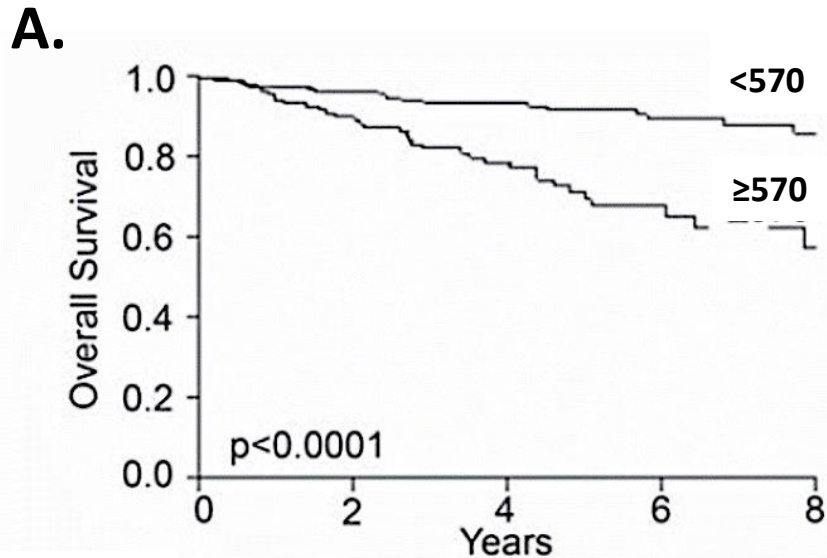
Stephen M. Ansell, MD, PhD

Professor of Medicine

Chair, Lymphoma Group

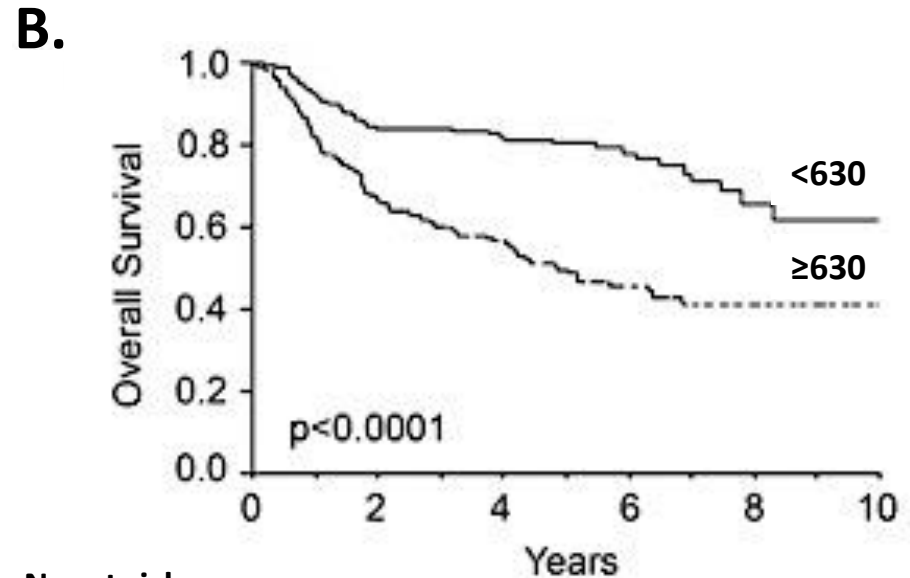
Mayo Clinic

# Peripheral blood monocyte numbers are associated with prognosis



<u>No. at risk</u>					
AMC low	225	198	131	71	39
AMC high	130	101	59	29	12

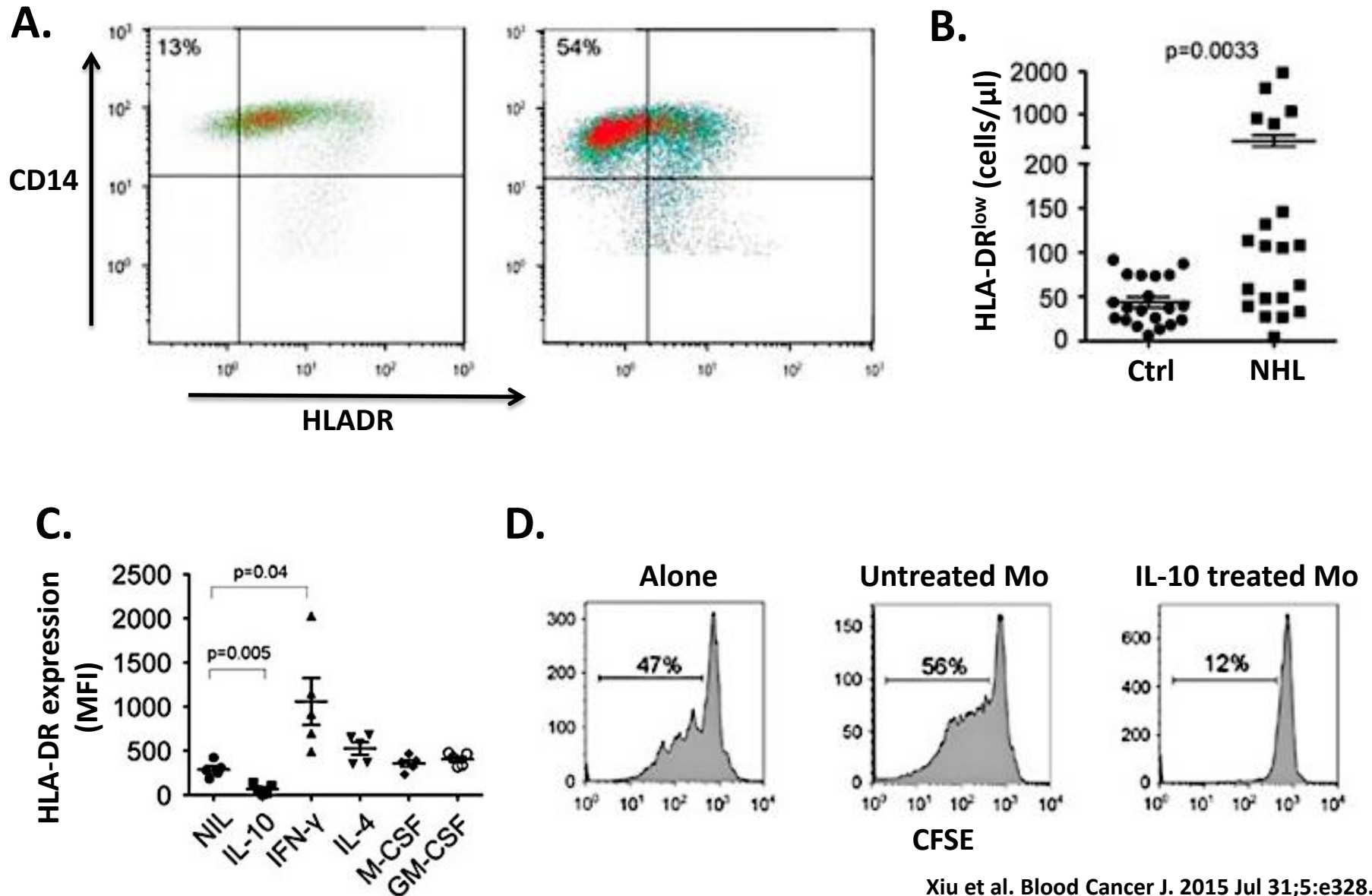
**Follicular lymphoma**



<u>No. at risk</u>						
AMC low	180	148	116	58	22	3
AMC high	186	123	77	36	14	4

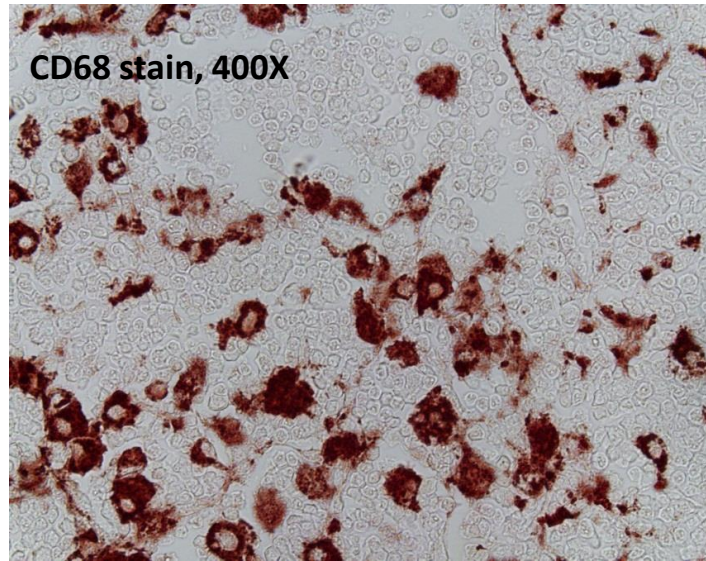
**DLBCL**

# CD14+HLA-DR<sup>low</sup> monocytes are associated with immunosuppression

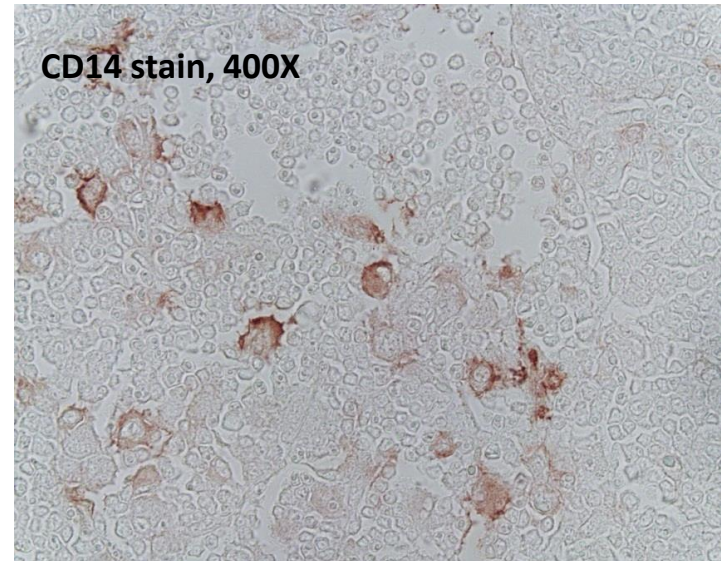


# Intratumoral monocytes have a different phenotype

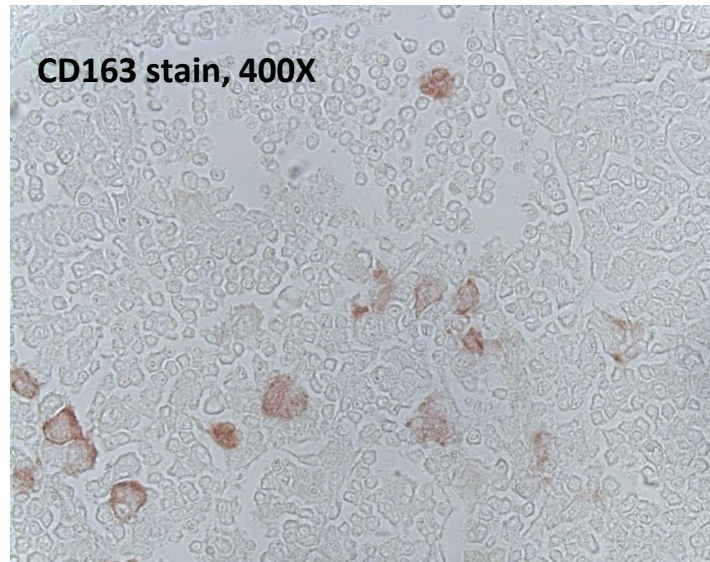
A.



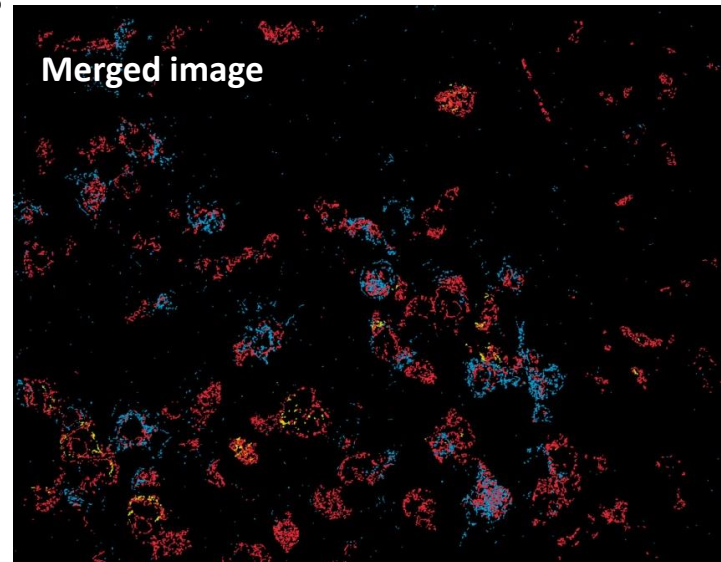
B.



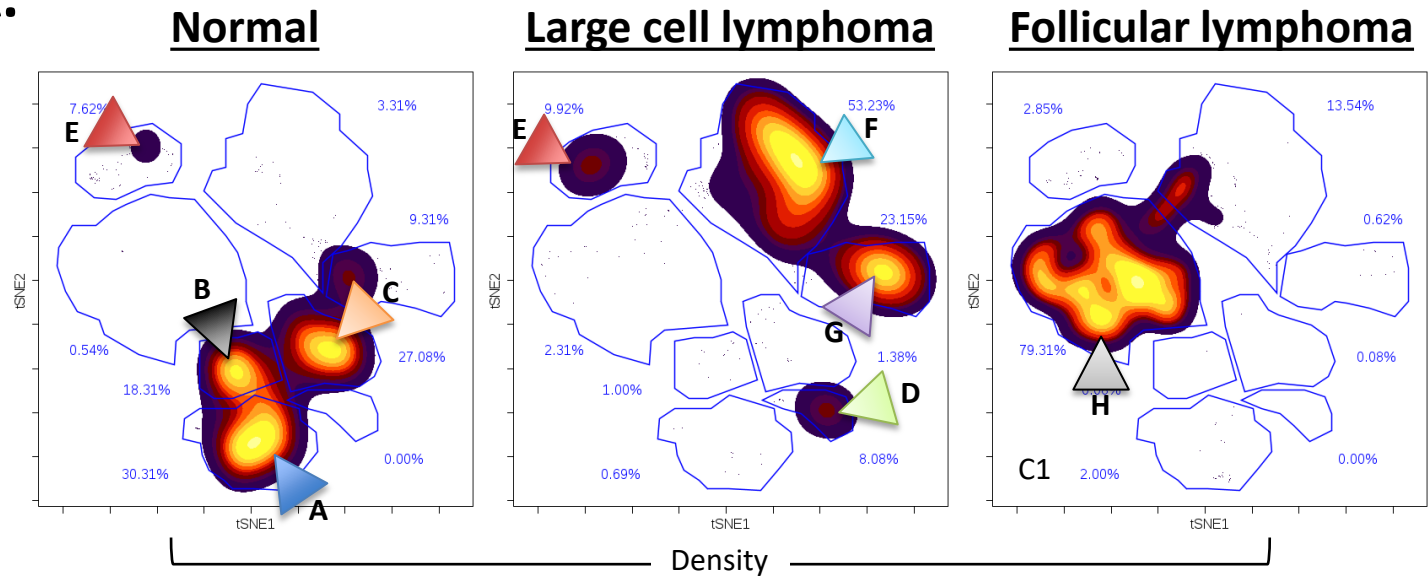
C.



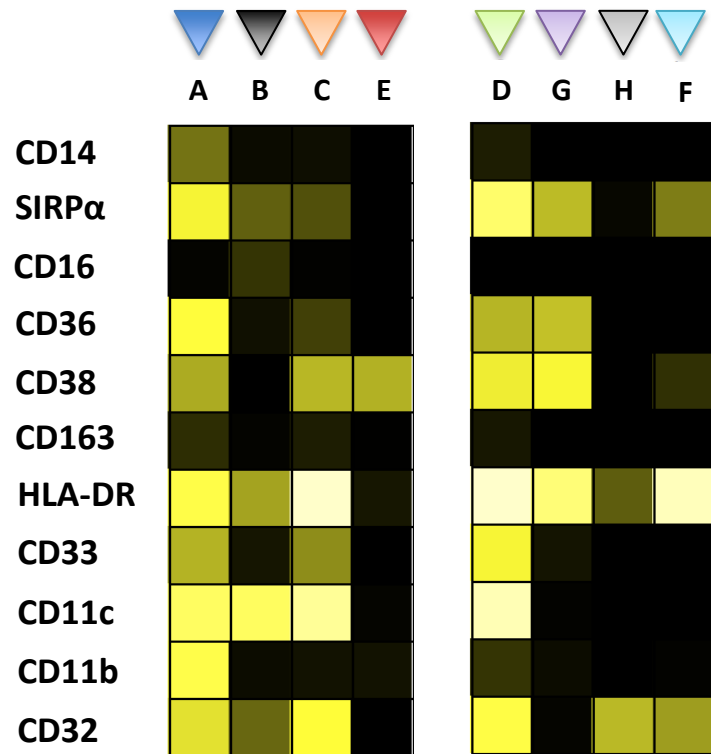
D.



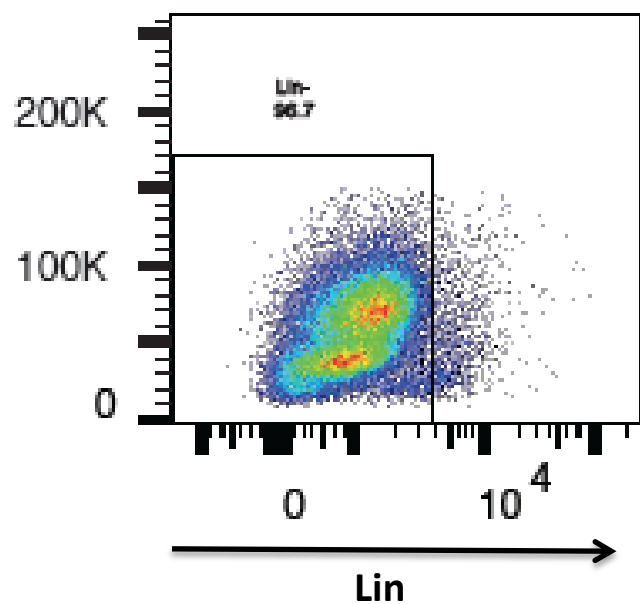
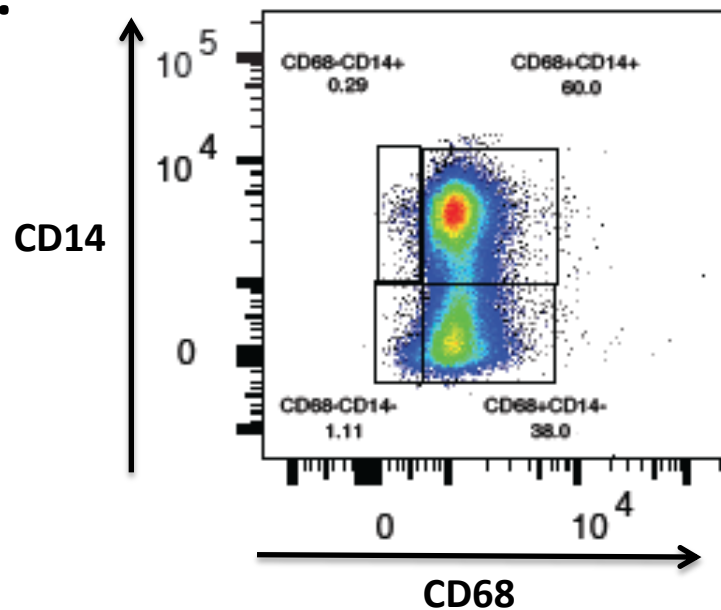
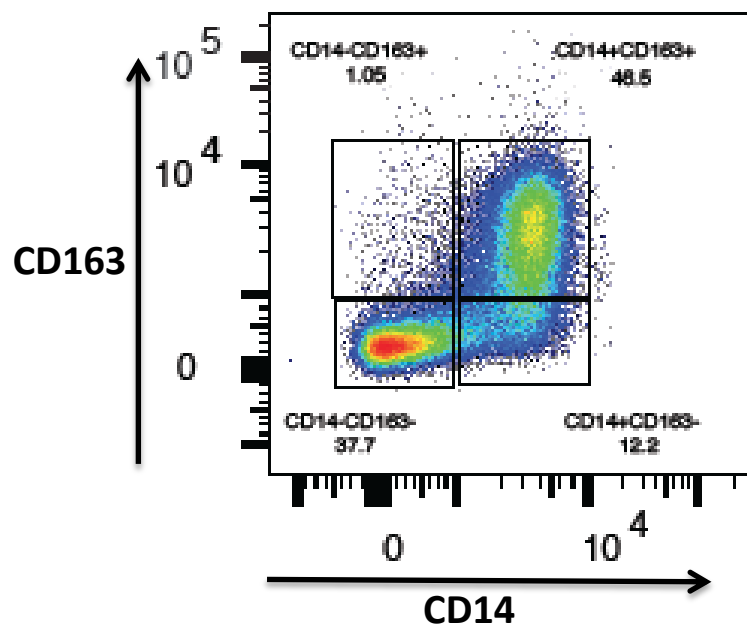
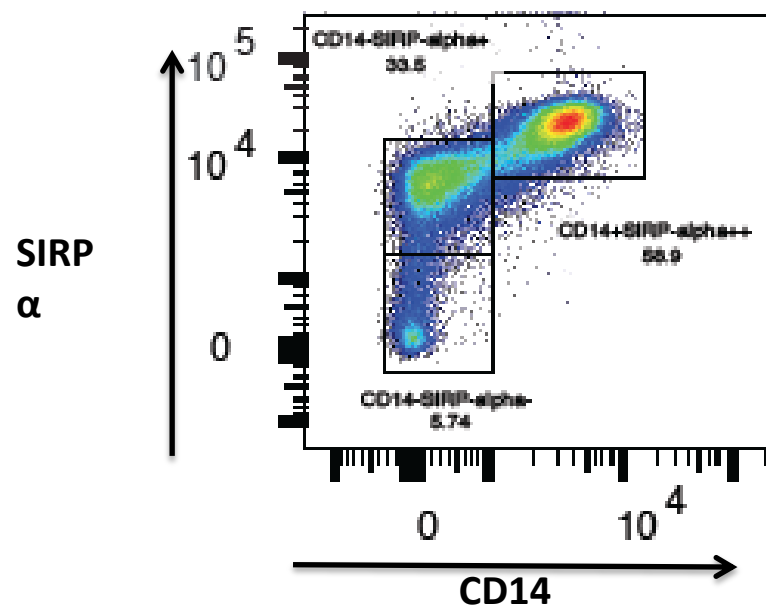
**A.**



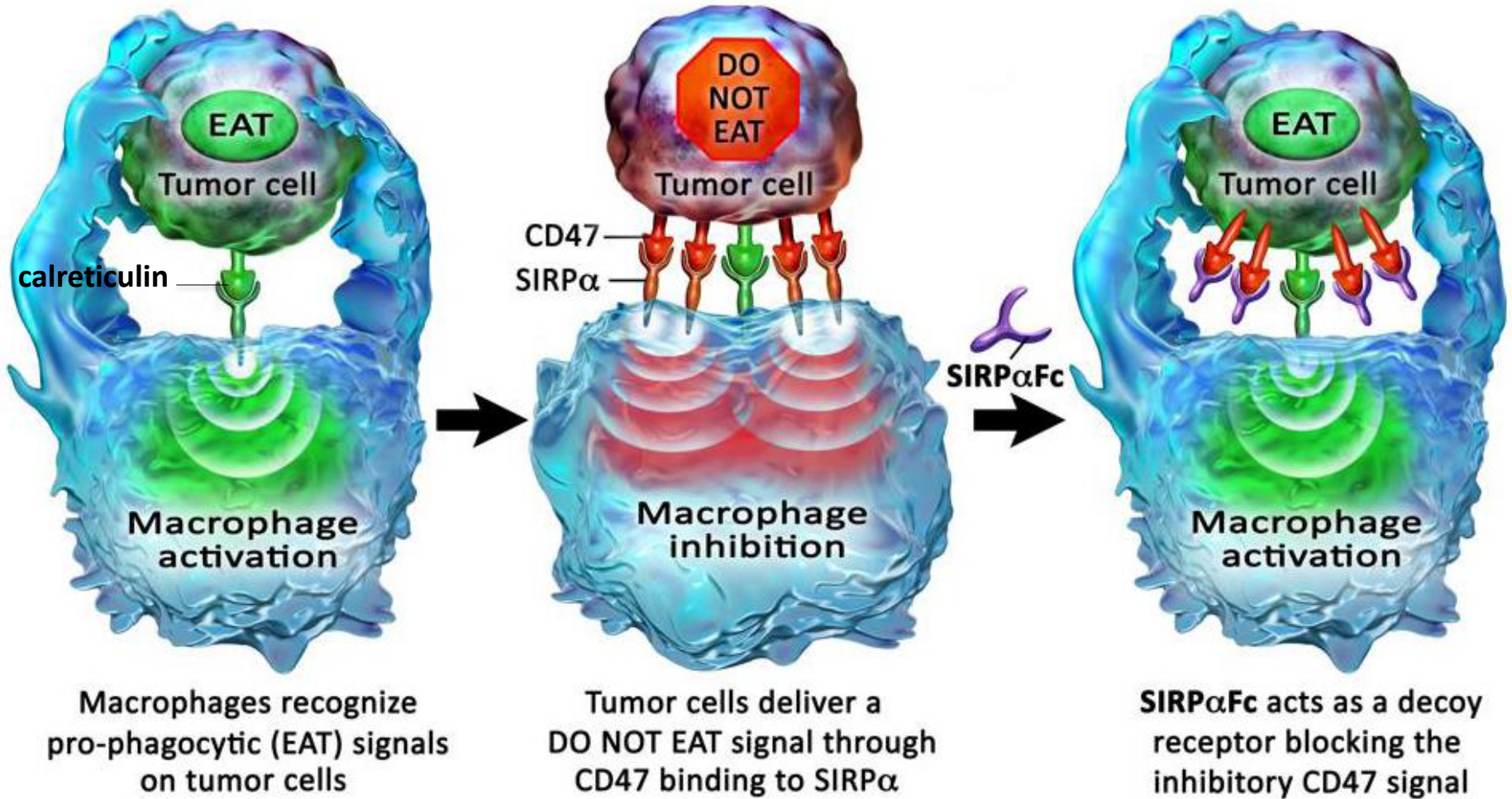
**B.**





**A.****B.****C.****D.**

# Mechanism of Phagocytosis



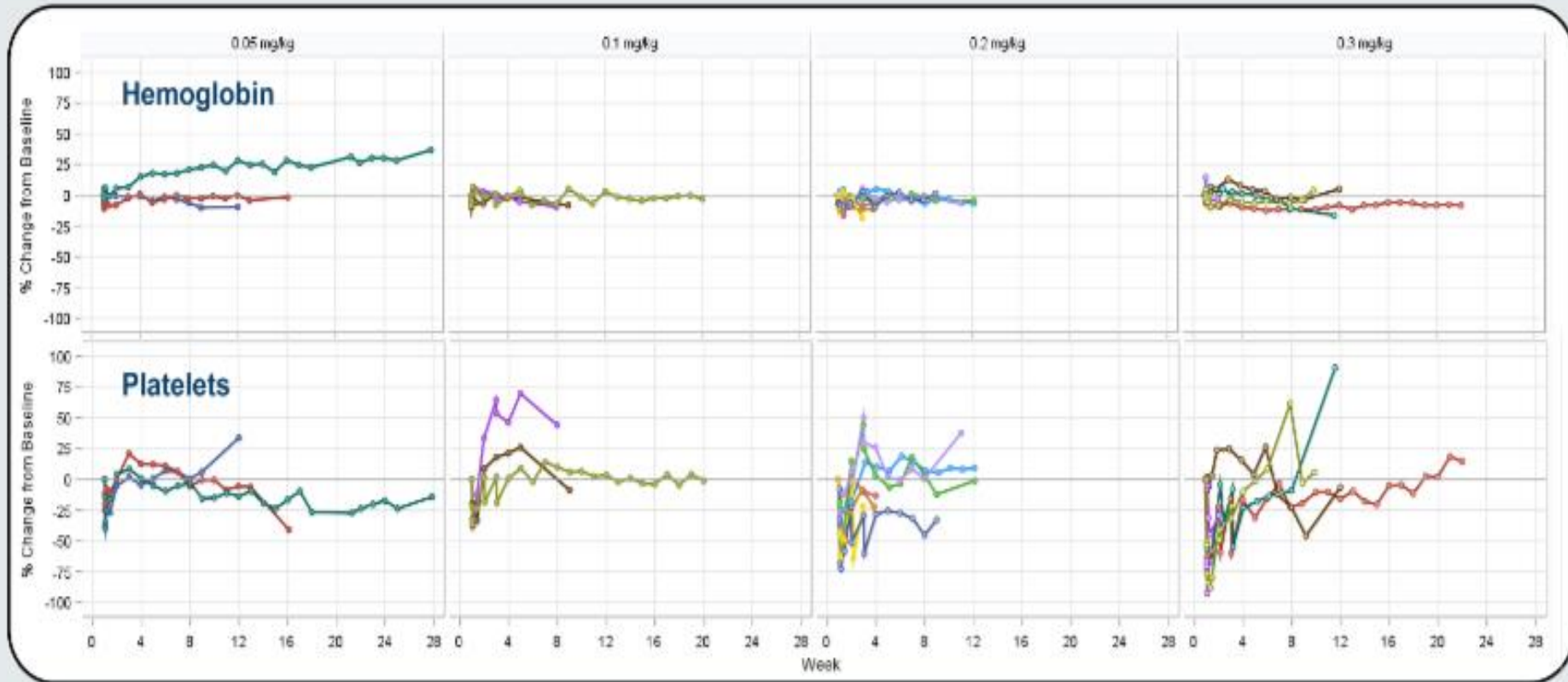
# A Phase 1 Study of TTI-621 in Patients with Relapsed or Refractory Hematologic Malignancies

All Adverse Events* (N=18)	All Grades	Grade 3	Grade 4
Infusion-related reaction	11 (61%)	-	-
Fatigue	9 (50%)	-	-
Diarrhea	7 (39%)	1 (6%) <sup>†</sup>	-
Headache	5 (28%)	-	-
Thrombocytopenia	4 (22%)	1 (6%)	2 (11%)
Chills	3 (17%)	-	-
Constipation	3 (17%)	-	-
Hypophosphatemia	3 (17%)	3 (17%)	-
Nausea	3 (17%)	1 (6%) <sup>†</sup>	-
Back pain	2 (11%)	-	-
Cough	2 (11%)	-	-
Myalgia	2 (11%)	-	-
Pruritus	2 (11%)	-	-
Pyrexia	2 (11%)	-	-
Rash	2 (11%)	-	-
Vomiting	2 (11%)	1 (6%) <sup>†</sup>	-

\*Adverse events of any causality in  $\geq 2$  patients <sup>†</sup>Unrelated self-limited gastroenteritis in 1 patient

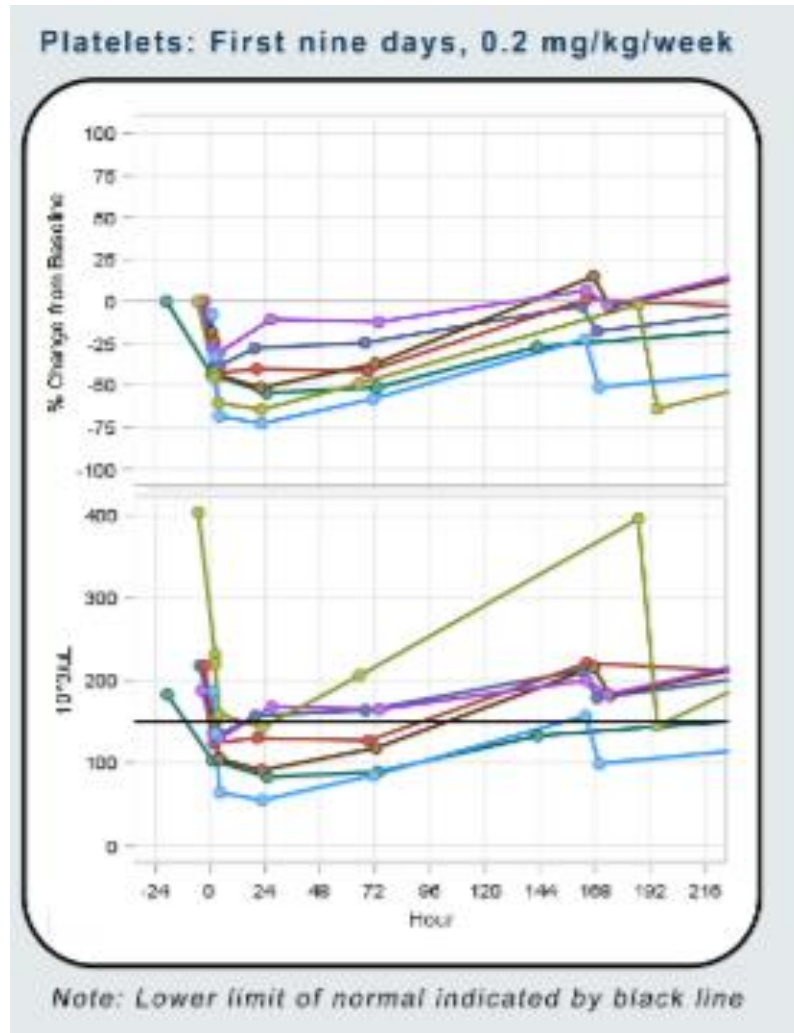


# A Phase 1 Study of TTI-621 in Patients with Relapsed or Refractory Hematologic Malignancies

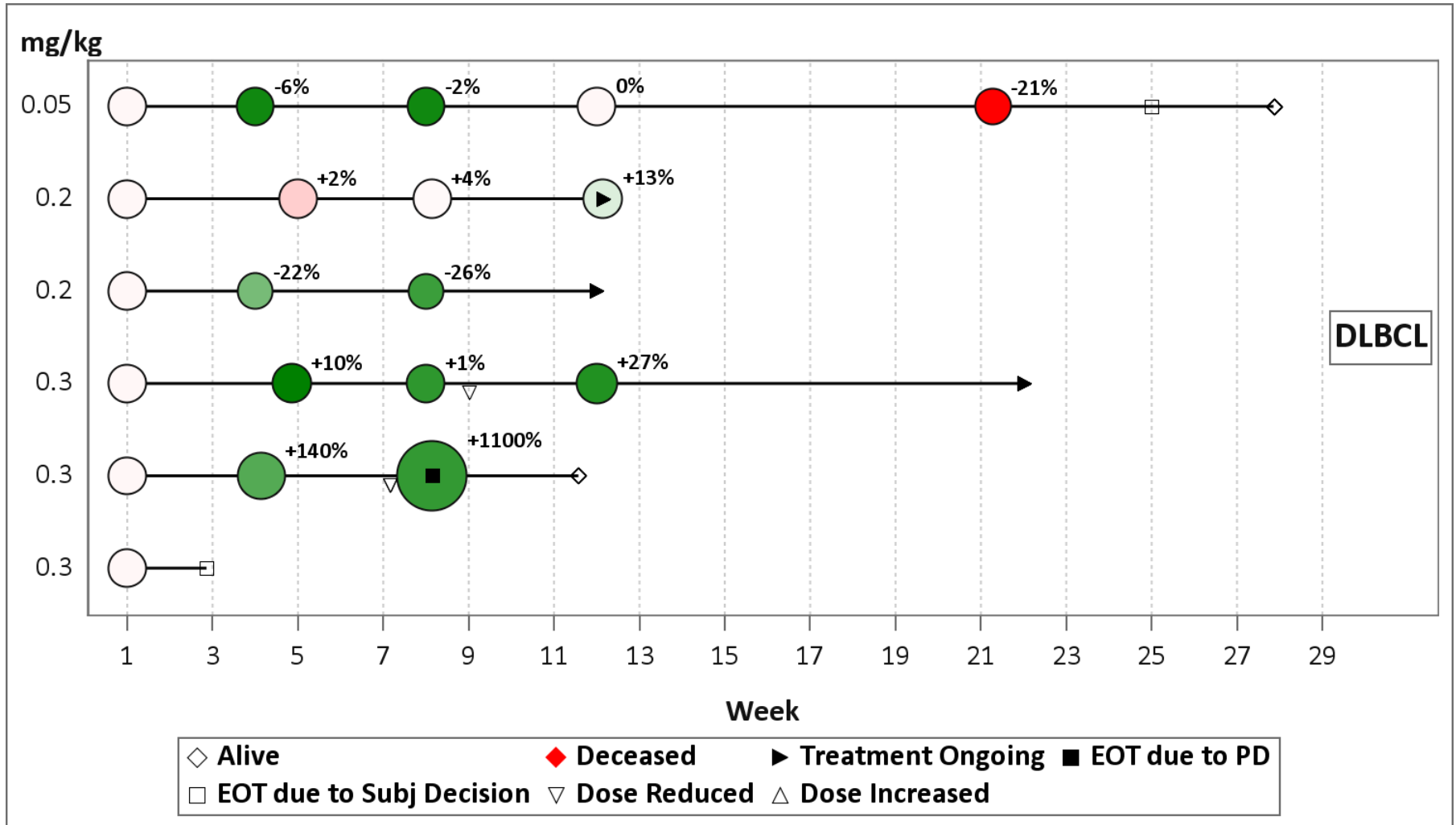


Note: pre-dose only sampling was employed after dose 3

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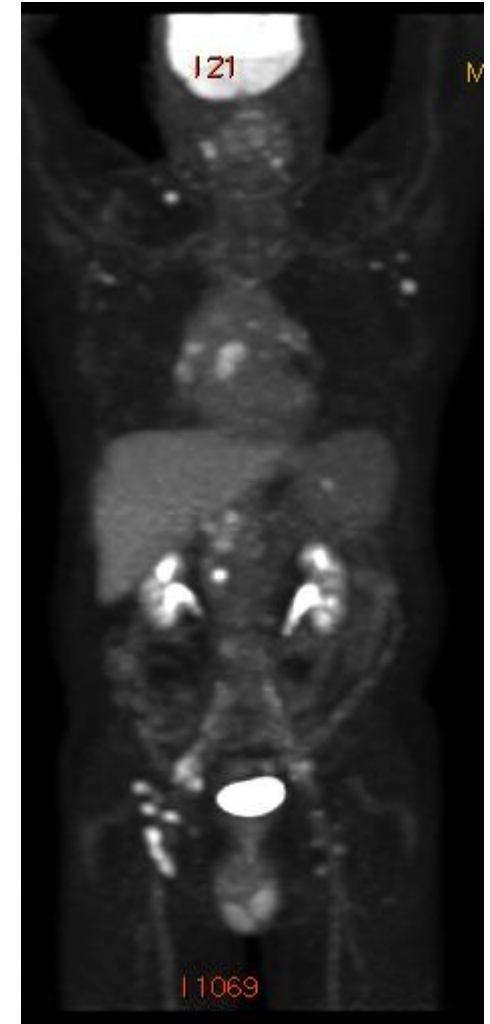
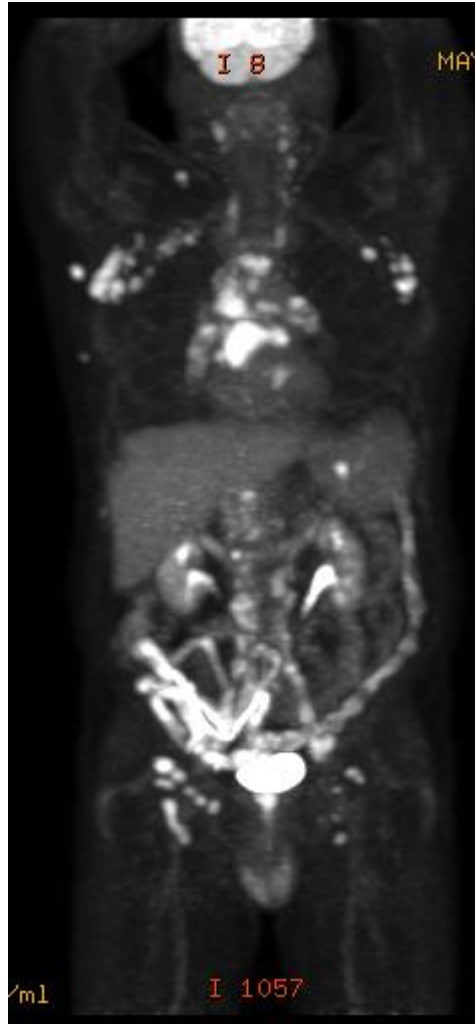
Nov 2016

Dec 2016

Jan 2017

SIRPa-Fc +  
Rituximab

Initial Dx –  
transformed  
lymphoma

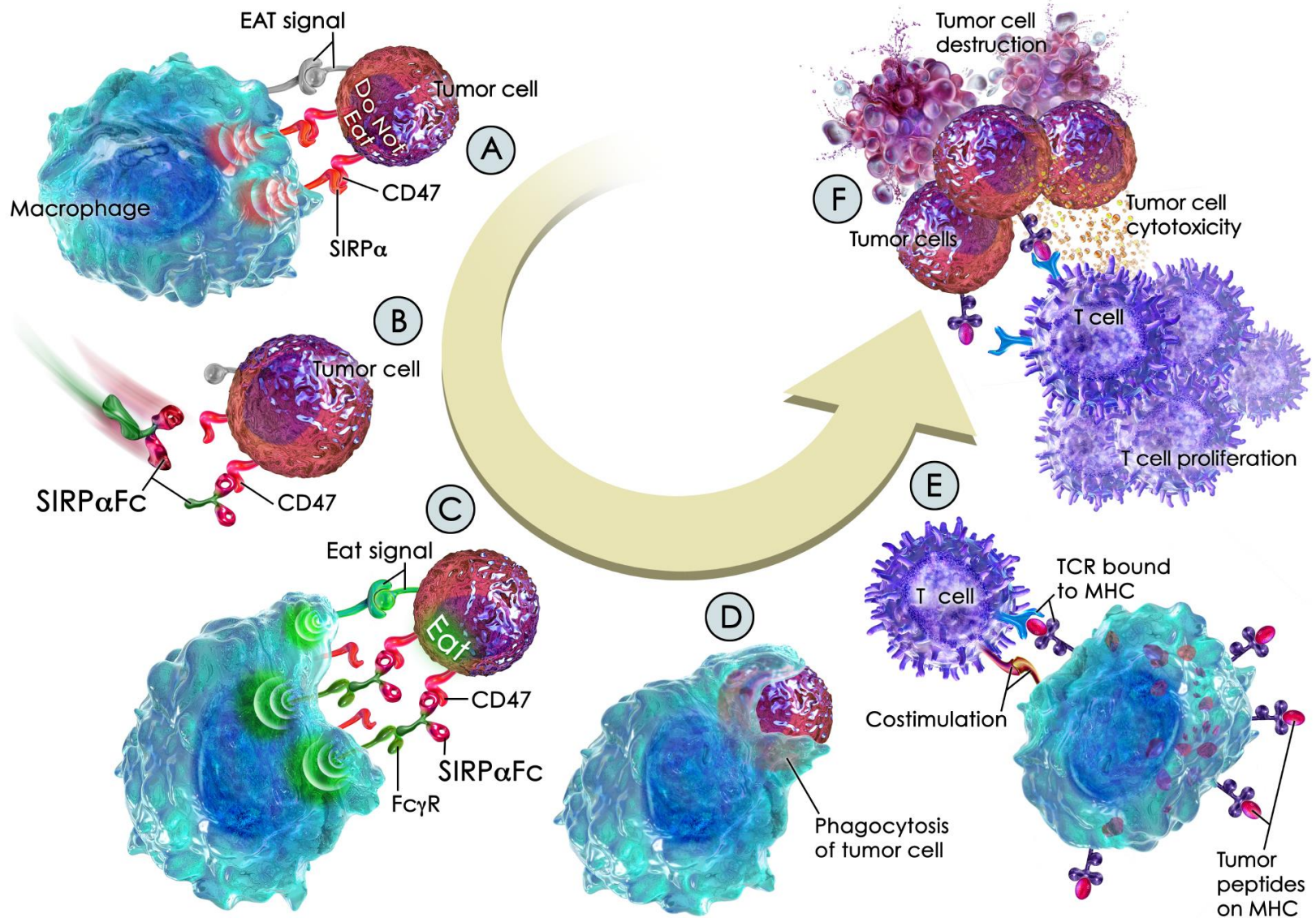


# **First-in-human, first-in-class phase I trial of the anti-CD47 antibody Hu5F9-G4 in patients with advanced cancers**

- Adults with solid tumors - Part A to determine the optimal Priming Dose, Part B to determine the optimal Maintenance Dose.
- 16 patients have been enrolled, 11 in Part A and 5 in Part B.
- In Part A, 1 mg/kg dose was selected as the Priming Dose.
- In Part B, the study is ongoing with the current cohort at 1 mg/kg followed by 10 mg/kg weekly.
- Hu5F9-G4-related AEs - anemia (11 G1, 5 G2), hyperbilirubinemia (5 G1, 3 G2, 1 G3), headache (9 G1, 1 G2), nausea (3 G1), and retinal toxicity (1 G2).
- Most AEs were associated with the Priming Dose and were reversible.
- Two patients (adenoid cystic ca) had stable disease for 16 and 8 months.



# Targeting CD47/SIRP $\alpha$ in Lymphoma



# Acknowledgements

## Lab members -

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