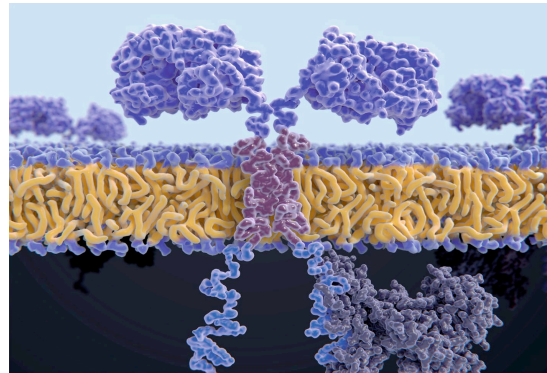




SANT PAU
Campus Salut
Barcelona



Hospital de
la Santa Creu i
Sant Pau

CART Cell Therapy for Hodgkin Lymphoma

Javier Briones

Hematology Service

Hospital Santa Creu i Sant Pau. Barcelona

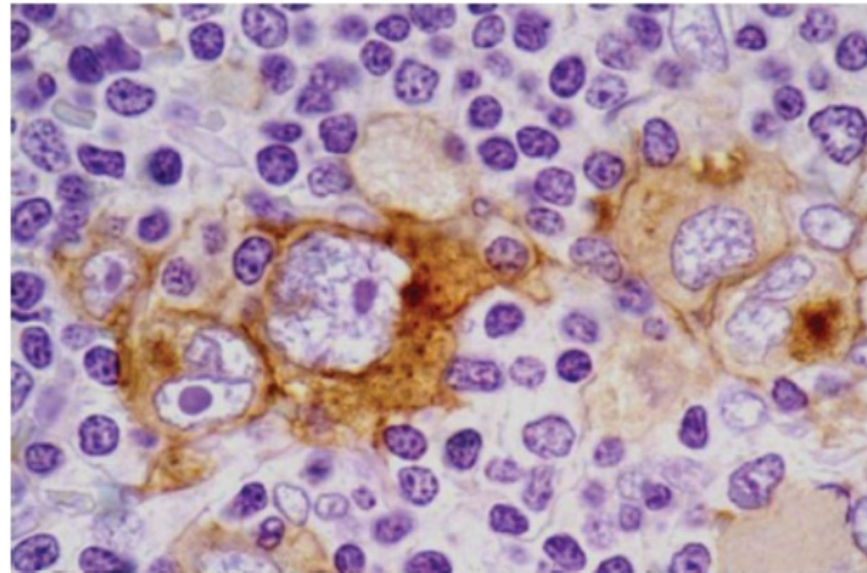


Disclosures

- None

CD30 as Target for Hodgkin Lymphoma

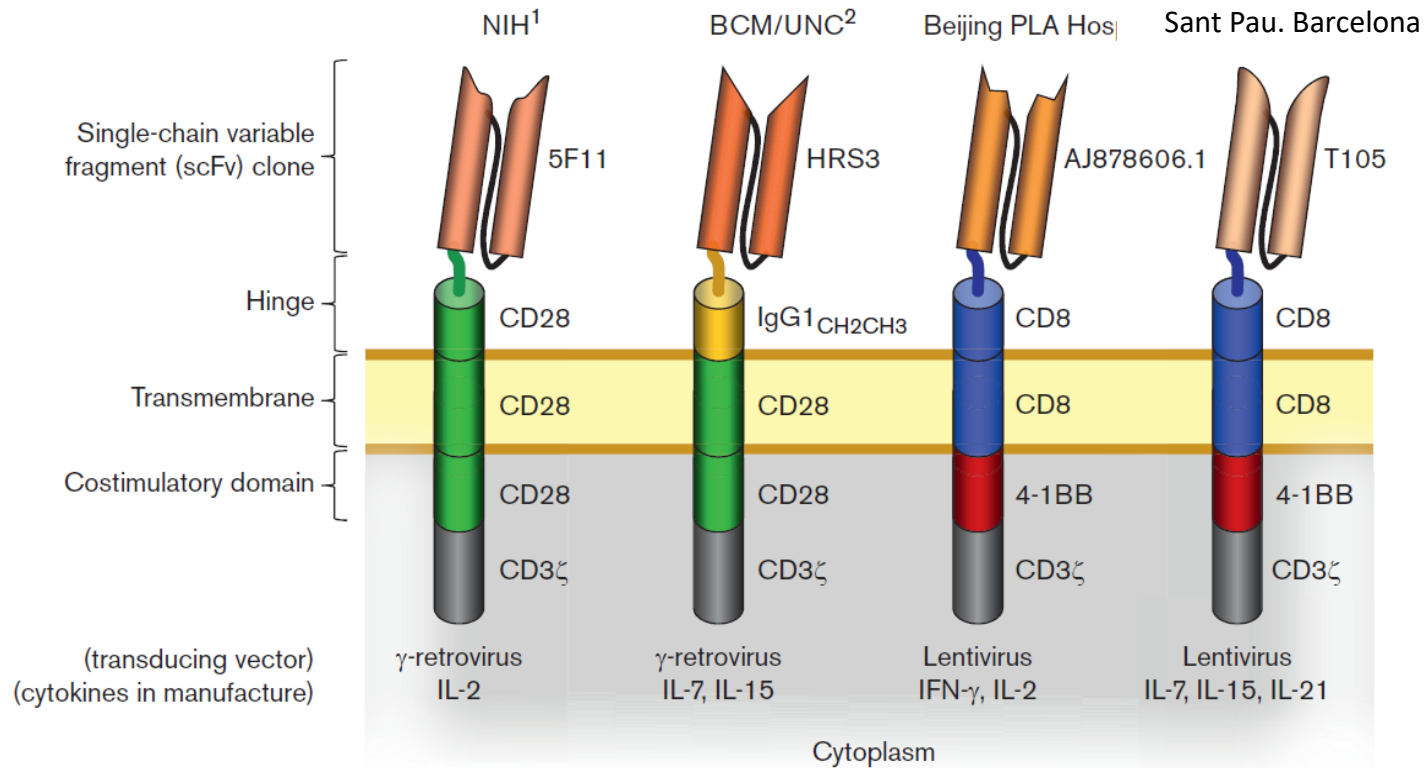
- Expressed in all malignant cells (Reed Sternberg's cells)
- Restricted expression in normal tissues:
 - Activated T, B, NK cells
- Expression retained on tumor cells after relapse
- CD30: ideal target for cellular immunotherapy



CART 30 for Hodgkin: summary of clinical trials

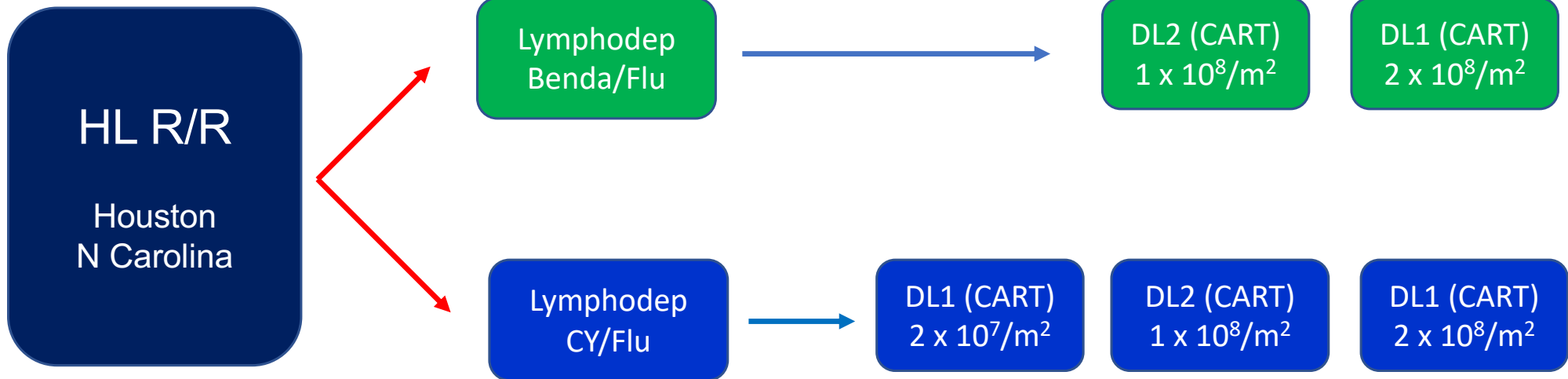
NCT Clin Trial	CAR design	Lymphodepletion	Dose	Institution
NCT04653649	CAR30-4-1BBz	Benda/Flu; Cy/Flu	2 x 10 ⁶ CART/Kg- 1 x 10 ⁷ CART/kg	H. Sant Pau. Barcelona
NCT02690545	CAR30-CD28z	Benda/Flu	2 x 10 ⁷ CAR/m ² 1-2 x 10 ⁸ CAR/m ²	U. North Carolina. USA
NCT02690545	CAR30-CD28z	Cy/Flu	2 x 10 ⁷ CAR/m ² 1-2 x 10 ⁸ CAR/m ²	Baylor College. Houston. USA
NCT03049449	CAR30-CD28z	Cy/Flu	0,3 x 10 ⁶ CART/Kg- 2x10 ⁷ CART/kg	National Cancer Institute. USA
NCT02259556	CAR30-4-1BBz	Cy/Flu, Gemcitabine, paclitaxel	1-3 x 10 ⁷ CART/kg	Pla Chinese Hospital. China
NCT03602157	CAR30-CCR4- CD28z	Benda/Flu	2 x 10 ⁷ -1 x 10 ⁸ CAR/m ²	U. North Carolina. USA

CAR30 Designs for Clinical Trials



Phase II CART30 Clinical Trial (Houston/UNC)

scFv anti CD30



Phase II CART30 Clinical Trial (Houston/UNC): Clinical Features

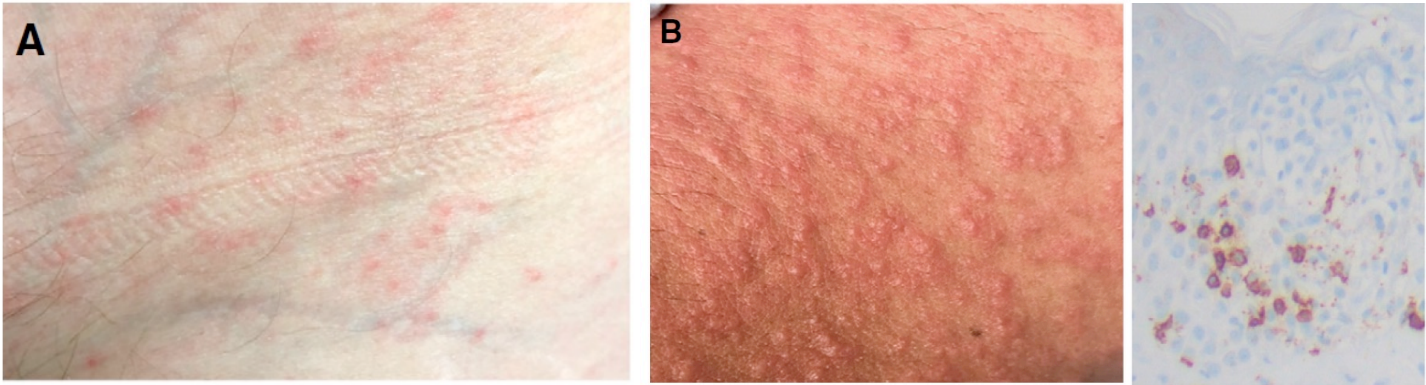
42 pts included

Histology	Median Age	MedianTx	ASCT	Allo	BV	CPI
NS: 76%	35 (17-69)	7 (2-23)	76%	24%	90%	81%

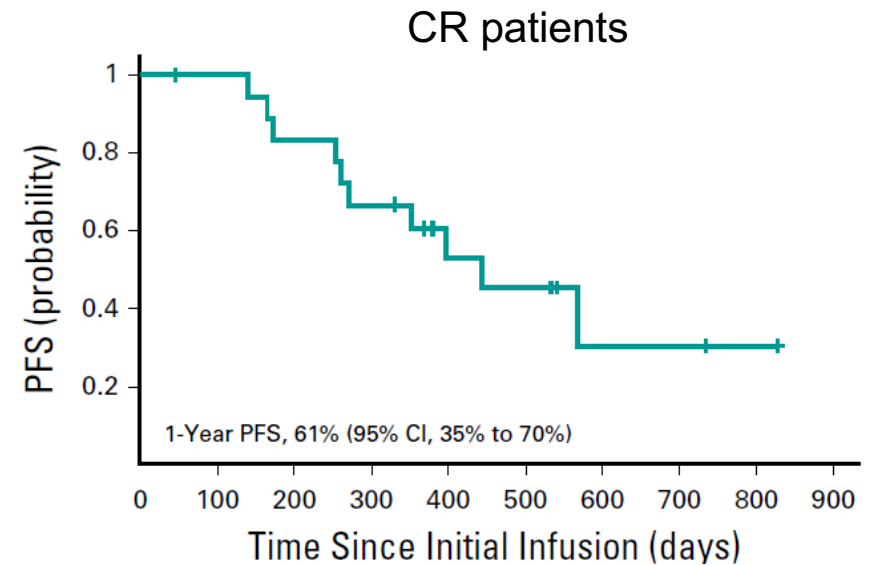
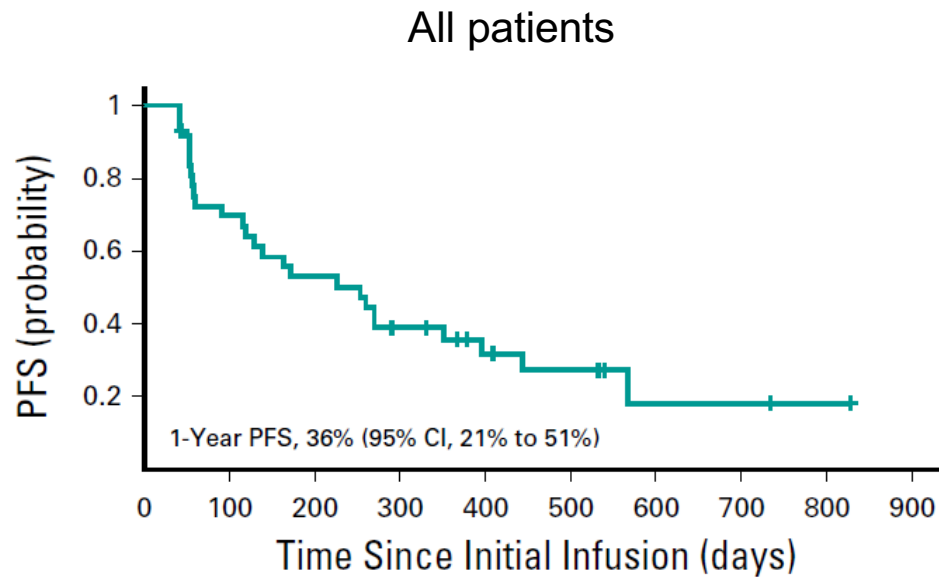
Phase II CART30 Clinical Trial (Houston/UNC): Efficacy and Toxicities

N= 32 patients evaluated for response

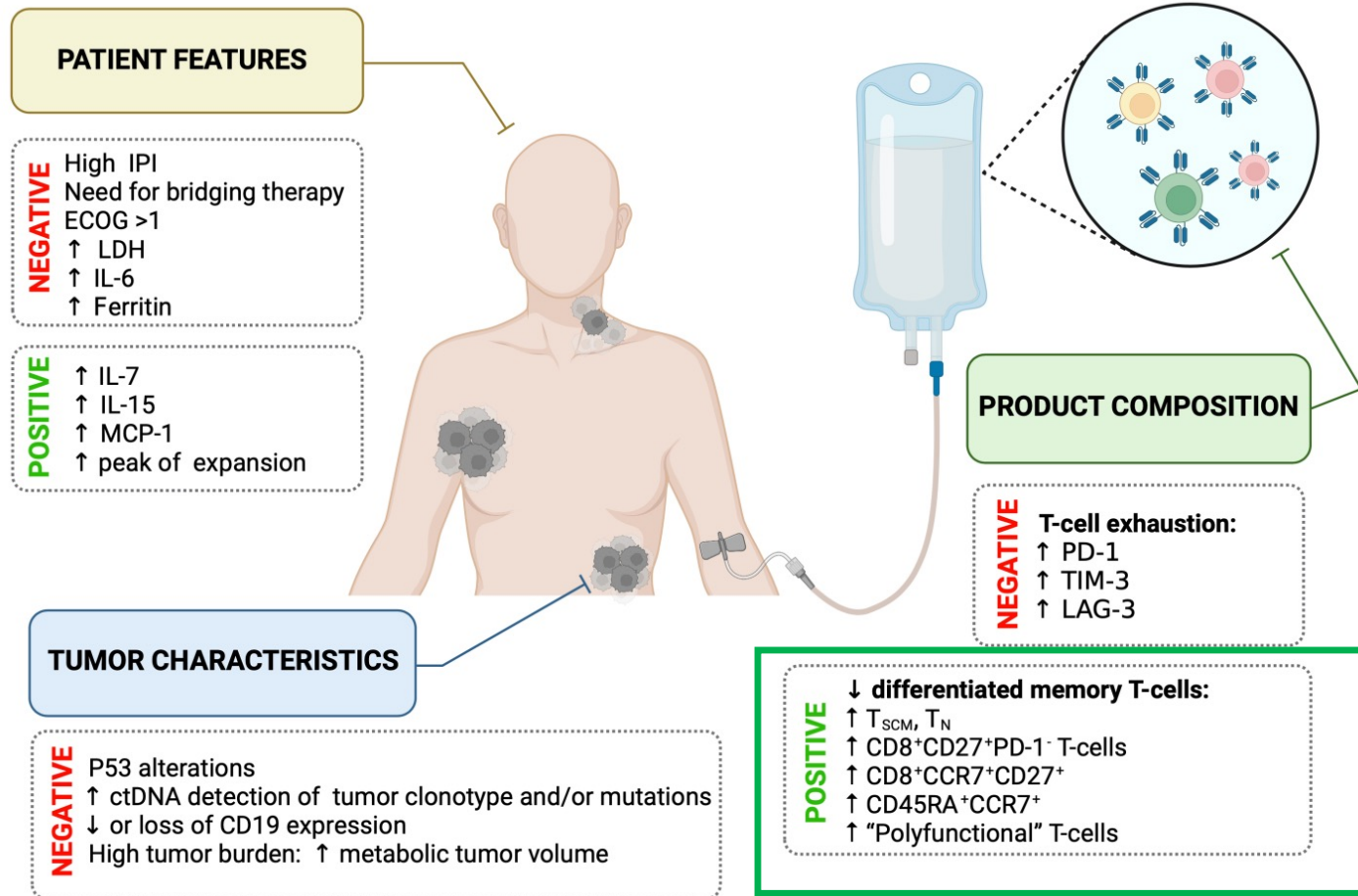
N	Overall Response	Complete Response	CRS	ICANS	Skin rash
32	23 (72%)	19 (59%)	24% (grade 1)	0	48%



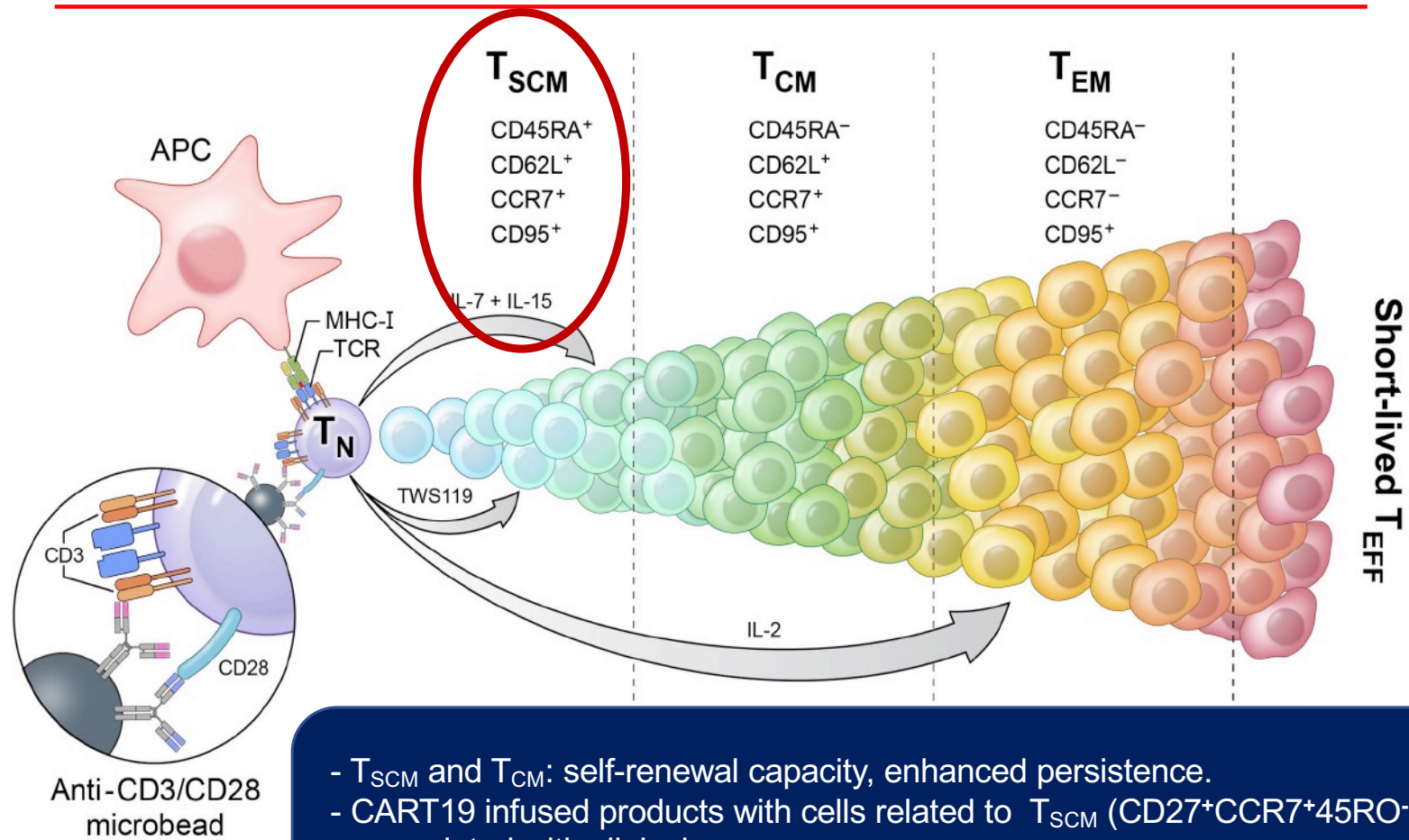
Phase II CART30 Clinical Trial (Houston/UNC): Survival



Factors Associated to CART Therapy Efficacy



Memory Stem T cells (T_{SCM}) for Adoptive Immunotherapy



- T_{SCM} and T_{CM} : self-renewal capacity, enhanced persistence.
- CART19 infused products with cells related to T_{SCM} (CD27⁺CCR7⁺45RO⁻) associated with clinical response.
- Proportion of T_{SCM} cells associated with CART19 expansion.

Gattinoni. Blood 2013

N. Restifo, L. Gattinoni. Curr Op Immunol 2013

Turtle C et al. Sci Transl Med 2016

Sommermeier D et al. Leukemia. 2015

Fraietta JA et al. Nature 2018

Academic HSP-CAR30 Clinical Trial: H. Sant Pau. Barcelona

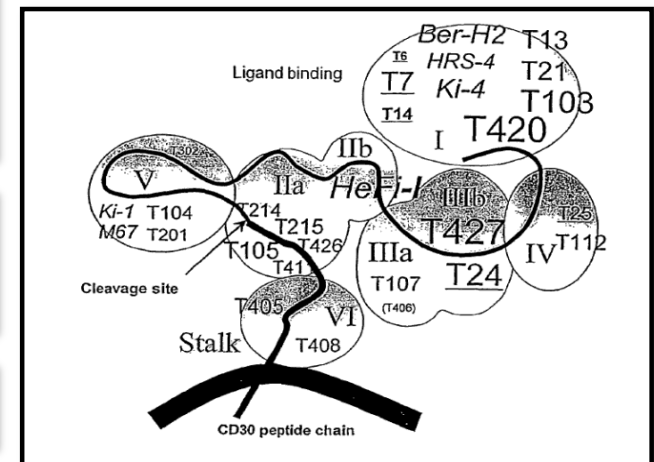


CAR30 construct: second generation CAR.

- CD30 scFv fused with the 4-1BB costimulation and the CD3ζ signal

The scFv recognizes a membrane-proximal epitope of the non-soluble CD30 protein

HSP-CAR30 enriched in memory T cells (T_{SCM} and T_{CM})



Alvarez-Fernandez/ Escribà-Garcia et al. Clin Transl Immunol. 2021
Caballero et al. Cancer Gene Ther. 2023

Clinical Trial with Academic CAR30 T cells (HSP-CAR30) (H. Sant Pau)

- Hodgkin relapse/refractory (chemo, ASCT, BV and anti-PD-1)
- CD30⁺ PTCL R/R (2 Tx lines or failure after ASCT)
 - ALCL and PTCL NOS/ AILD CD30⁺
- Phase I/IIa study
 - Stage I: 3 cohort, dose escalation, sequential treatment
 - Stage II: patients treated at MTD



SANT PAU
Campus Salut
Barcelona

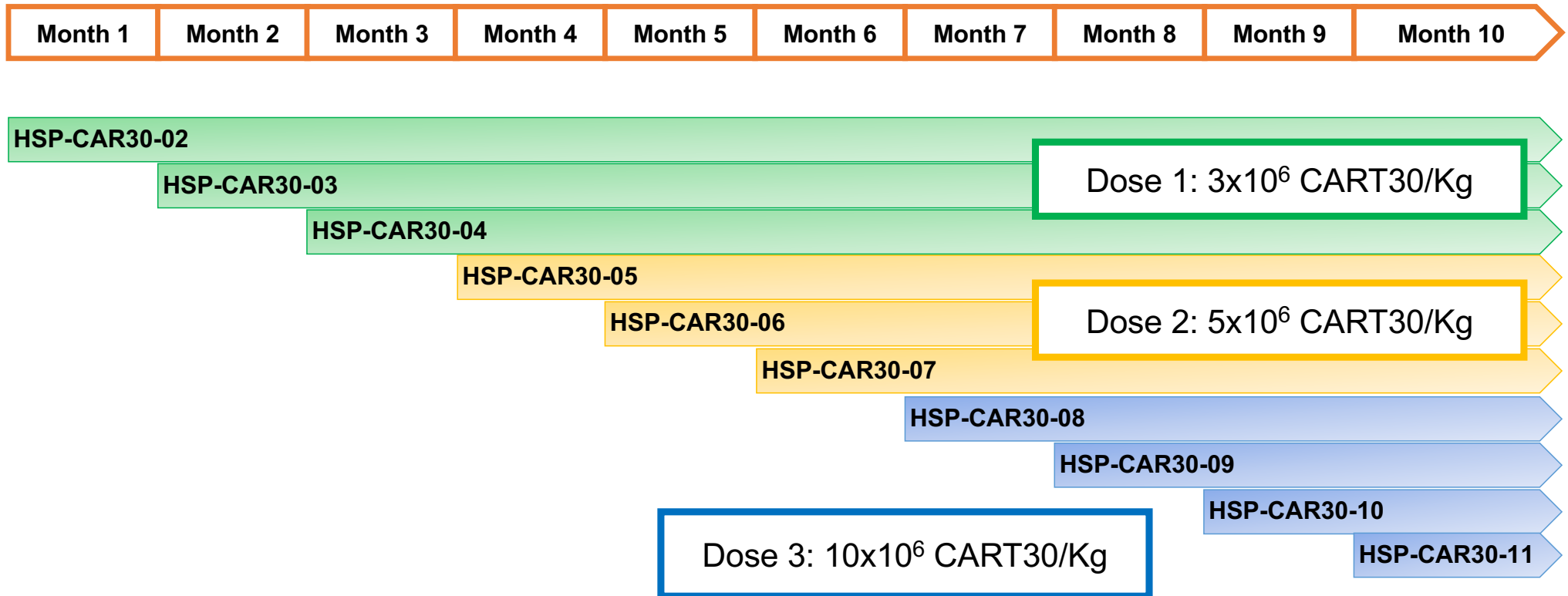
EudraCT: 2019-001263-70

NCT04653649

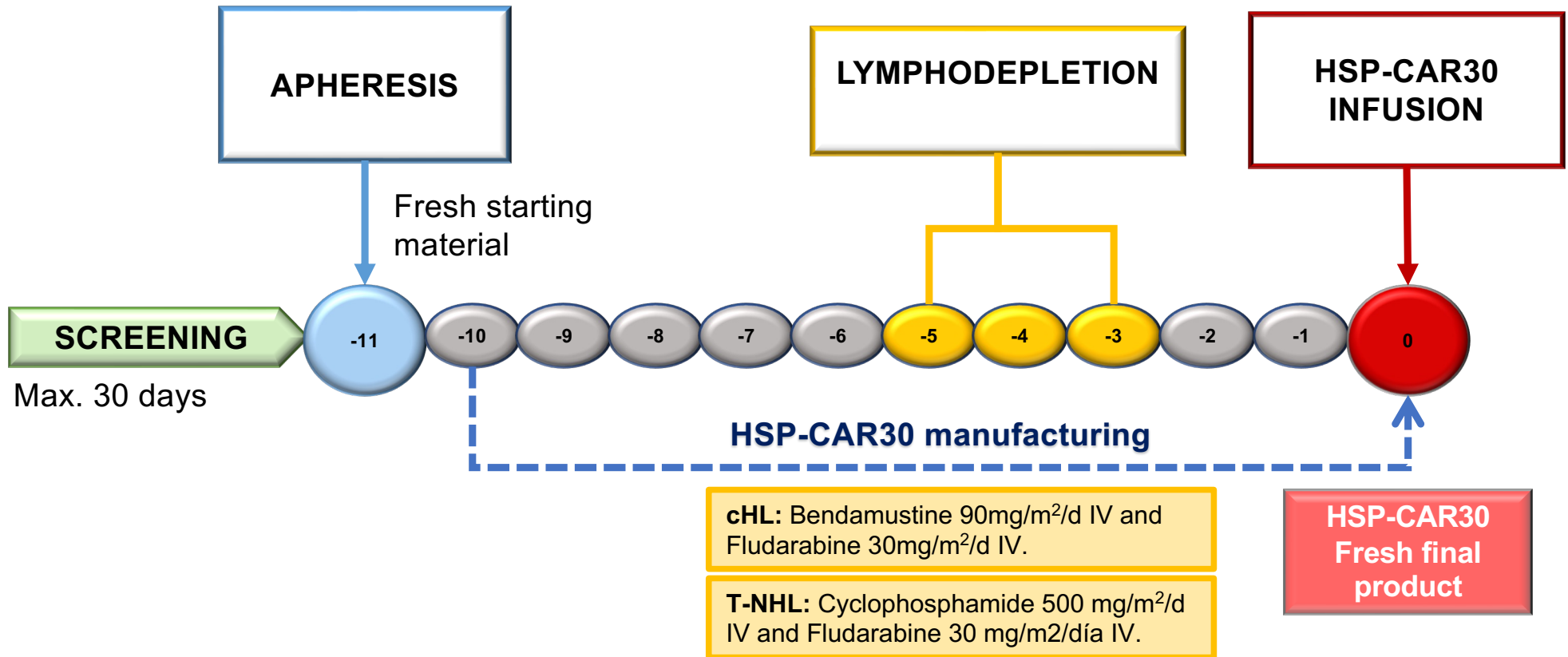


Hospital de
la Santa Creu i
Sant Pau

Phase I study (3+3 design). Dose escalation, sequential treatment



Treatment Procedures Design and HSP-CAR30 Manufacturing



Patient Demographics and Disease Features

	PATIENT	AGE (years)	DIAGNOSIS	STAGE	EXTRANODAL SITES	PRIOR LINES N°	PRIOR ASCT	REFRACTORY PRIOR LINE	REF. TO BV	REF TO Anti-PD1
	HSP-CAR30-01	38	HL	IIA	-	8	Yes	Yes	Yes	Yes
DOSE 1	HSP-CAR30-02	42	HL	IVA	SC tissue, muscle, bone	4	No	Yes	No	Yes
	HSP-CAR30-03	65	T-NHL	IVA	GI (stomach), lung	7	Yes	No	Yes	No
	HSP-CAR30-04	49	HL	IIA	-	5	Yes	Yes	No	Yes
DOSE 2	HSP-CAR30-05	48	HL	IIA	-	4	Yes	No	No	No
	HSP-CAR30-06	43	HL	IVA	Bone, lung	5	No	Yes	Yes	Yes
	HSP-CAR30-07	38	HL	IVB	Bone	4	No	Yes	Yes	Yes
DOSE 3	HSP-CAR30-08	63	HL	IVA	Bone	5	No	Yes	Yes	Yes
	HSP-CAR30-09	65	T-NHL	IVA	Skin, SC tissue, muscle	3	Yes	No	Yes	-
	HSP-CAR30-10	65	HL	IVA	Bone	5	Yes	No	Yes	No
	HSP-CAR30-11	21	HL	IIIA	-	4	Yes	Yes	No	Yes

Median prior lines: **5** (3 –7)

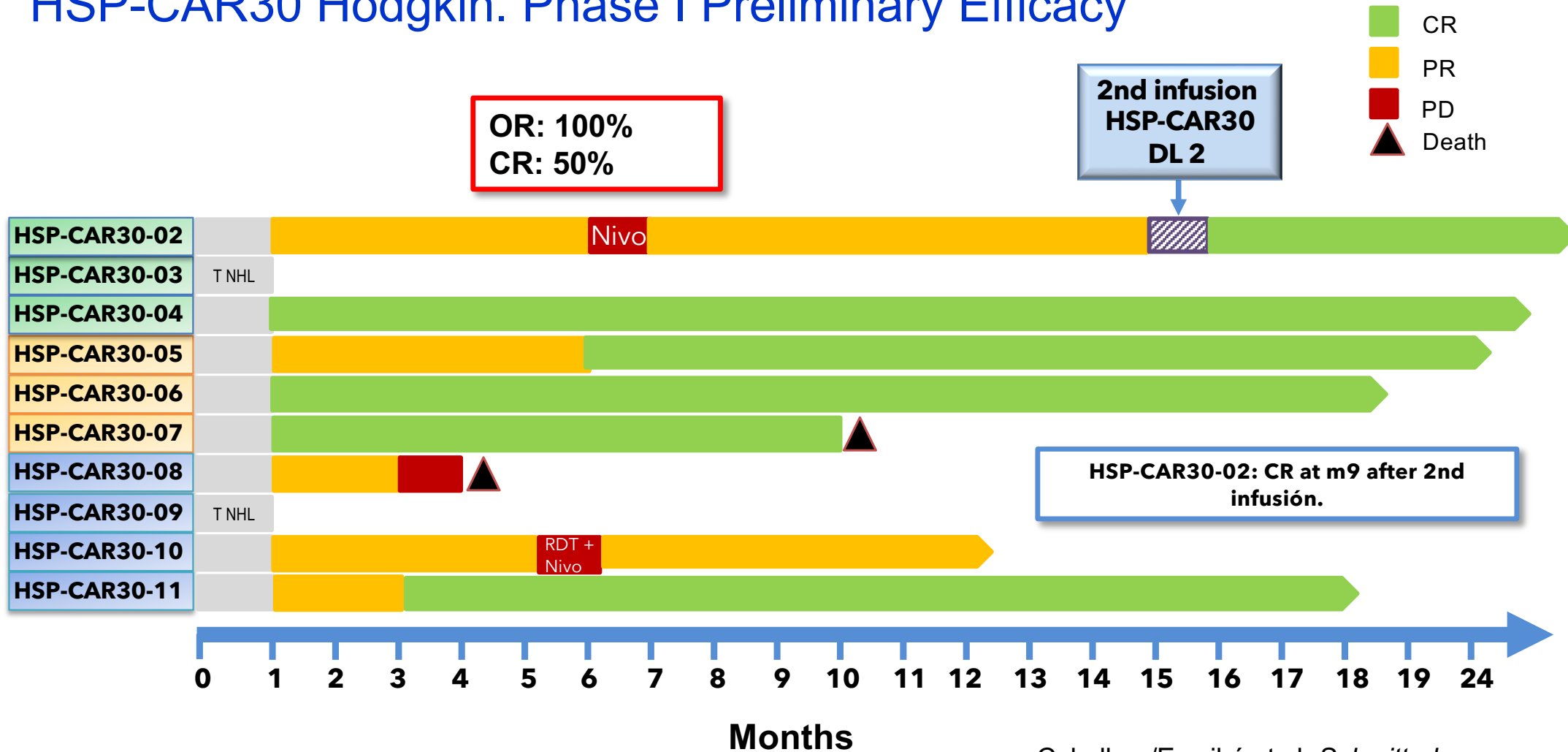
Refractory to prior line: **6/10**

Previous ASCT: **6/10**

HSP-CAR30: Phase I Safety

Patient	CRS (Grade)	CRS onset day	CRS duration (days)	ICANS (Grade)	Rash (BS*%)
HSP-CAR30-02	Yes (1)	1	1	No	No
HSP-CAR30-03	Yes (1)	21	2	No	Yes (27)
HSP-CAR30-04	No			No	No
HSP-CAR30-05	No	-	-	No	No
HSP-CAR30-06	No	-	-	No	No
HSP-CAR30-07	Yes (1)	0	2	No	Yes (18)
HSP-CAR30-08	No	-	-	No	Yes (45)
HSP-CAR30-09	Yes (1)	1	2	No	Yes (36)
HSP-CAR30-10	Yes (1)	0	3	No	No
HSP-CAR30-11	Yes (1)	2	2	No	No

HSP-CAR30 Hodgkin. Phase I Preliminary Efficacy



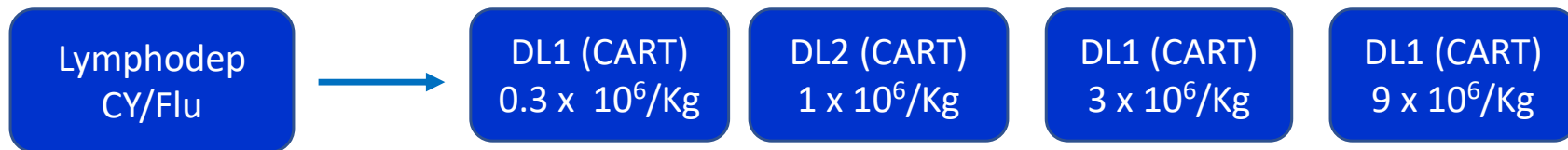
Caballero/Escribá et al. *Submitted*

Phase I CART30 Clinical Trial: NCI study

scFv anti CD30 (5F-11)



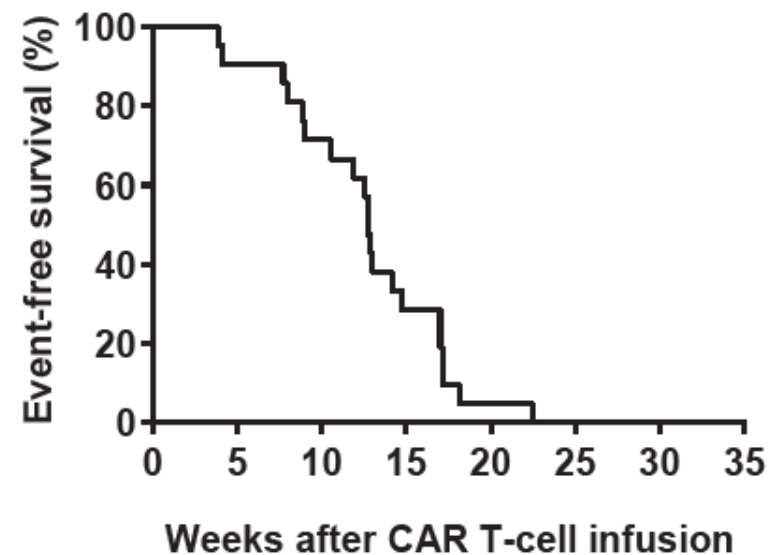
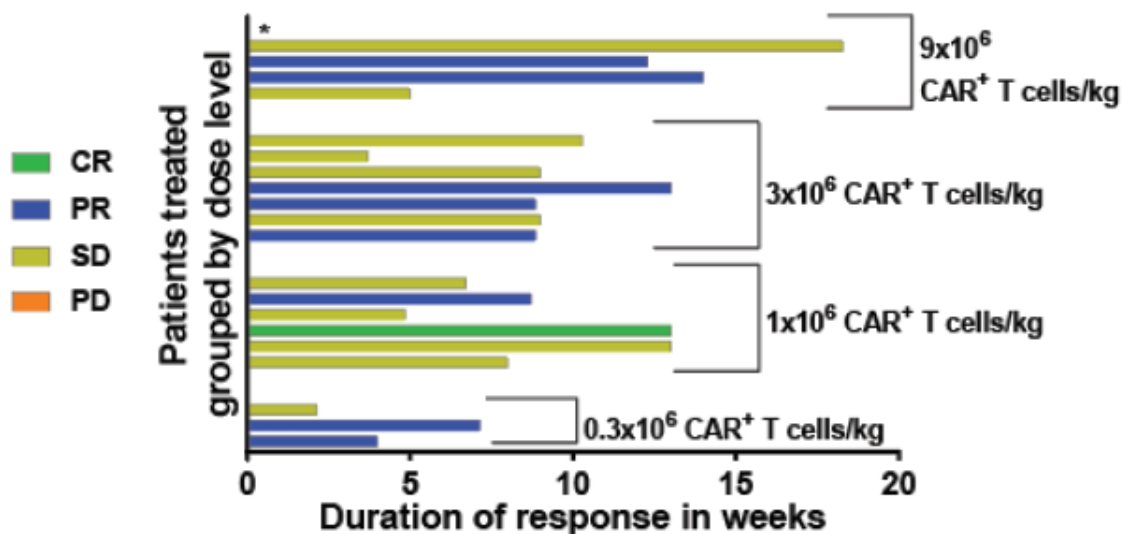
20 pts included



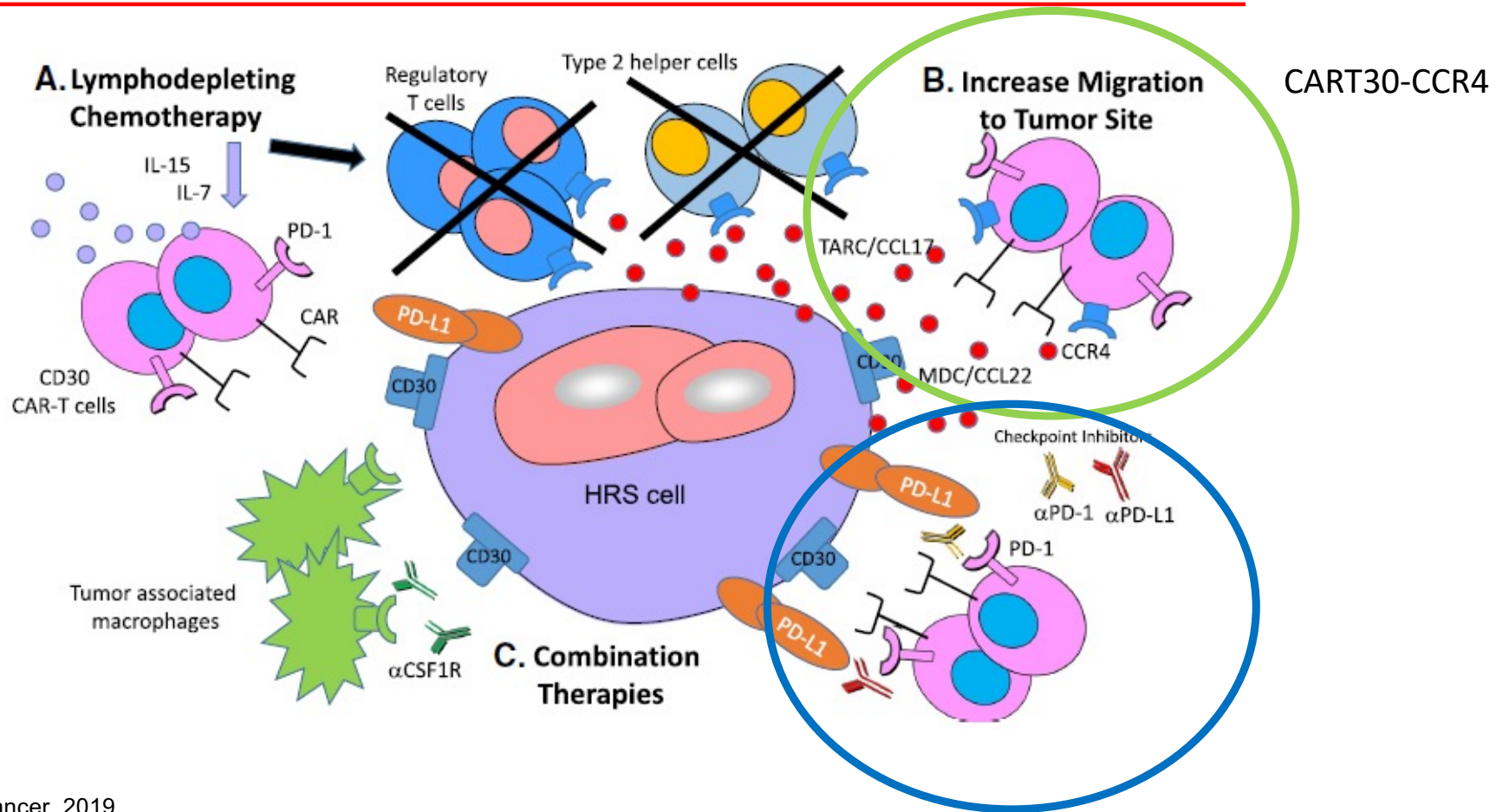
Phase I CART30 Clinical Trial: NCI study

Histology	MedianTx	OR	CR	CRS	ICANS	Skin Tox
cHL (20)	7	43%	5% (1 pt)	52% (only 1 gr 3)	24% (gr 2)	43% (10% gr 3)

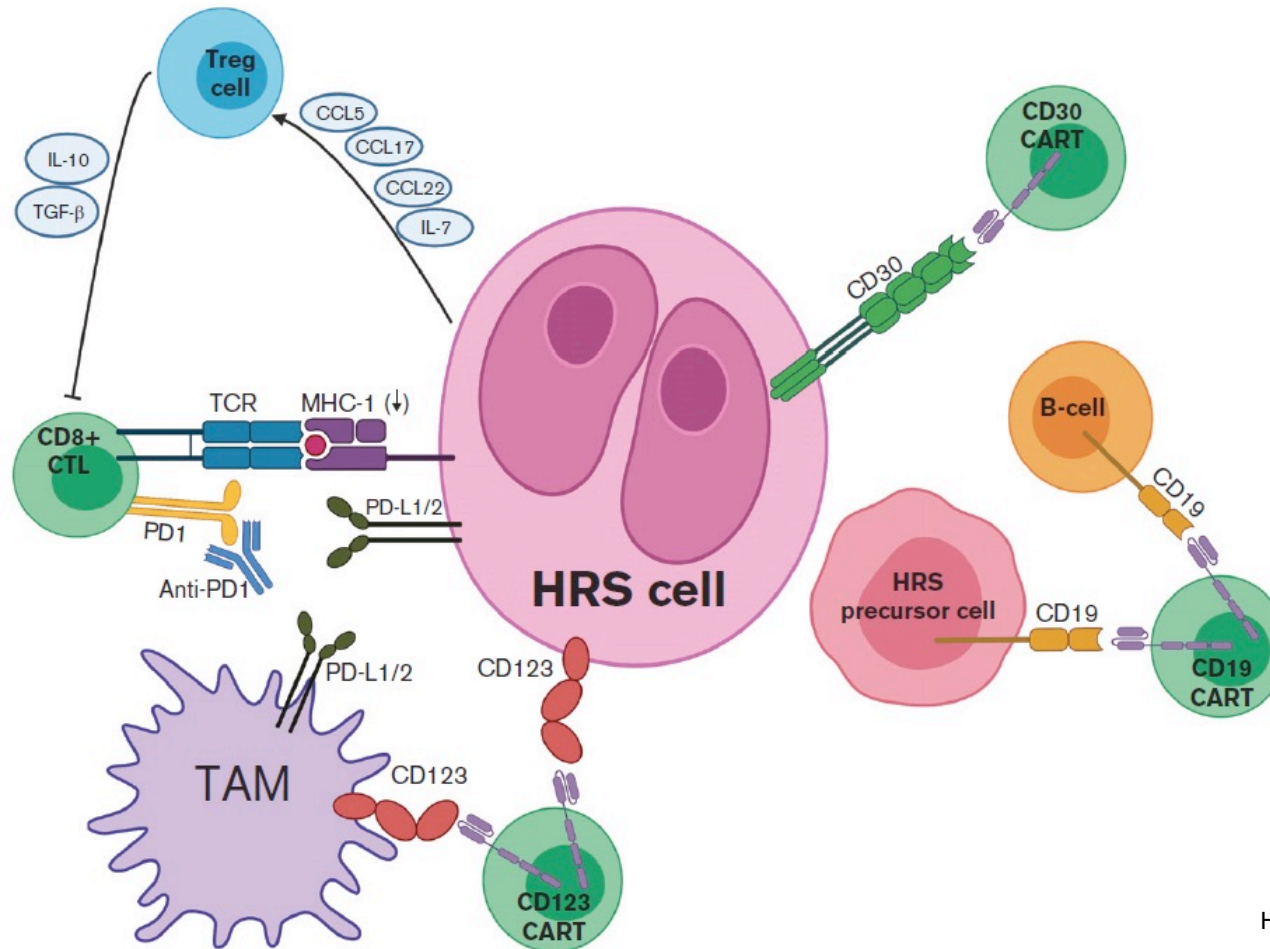
Phase I CART30 Clinical Trial: NCI study



Improving CART30 Efficacy



CART Cell Therapy for cHodgkin: additional Targets





Hematology

Javier Briones
Ana Caballero
Irene G^a-Cadenas
Albert Esquirol
Iria González
Olga Aso

UMCAR-SP

Jordi Mancebo (ICU)
J. Carlos Suarez (ICU)
Estela Moreno
(Pharmacy)
Mireia Ribas (Pharmacy)
Luis Querol (Neuro)
Lorena Martin (Neuro)

Research Institute

Marta Mitjà
Agostina Robledo
Matilde Parreño
Jordi Surralles

Microbiology

Ferran Navarro
Raul Altaba

BST

Luciano Rodríguez
Laura Medina
Sergi Querol

CELL IMMUNOTHERAPY AND GENE THERAPY GROUP **HEMATOLOGY SERVICE.** **RESEARCH INSTITUTE. HOSPITAL SANT PAU**



Laura
Escribà

Ana
Caballero

Javier
Briones

Rosanna
Montserrat

Paula
Pujol

Ferrán
Balbastre

María
Guardiola

Carmen
Alvarez

Eva
Escudero

Cristina
Ujaldón