



Ponencia inaugural

Terapias avanzadas en oncología: de los TILs al CAR-T (y viceversa)



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Hospital Clínic de Barcelona (HCB-FCRB) - IDIBAPS /

Immunotherapy platform Hospital Sant Joan de Déu-HCB

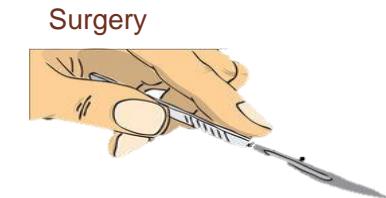
mjuan@clinic.cat

NH Collection Gran Hotel. Zaragoza, 16-09-2023; 17:00 h (20 min).

CONFLICT OF INTEREST - DISCLOSURES

*No conflict by commercial interests or relationship with companies, except in what corresponds to **educational talks** sponsored by some companies and specific participations (2 meetings 2 years ago at least) as member of an Oncology Advisory Board of Grifols & Cytometry board of BD Biosciences, no-related with CAR-T therapy.*

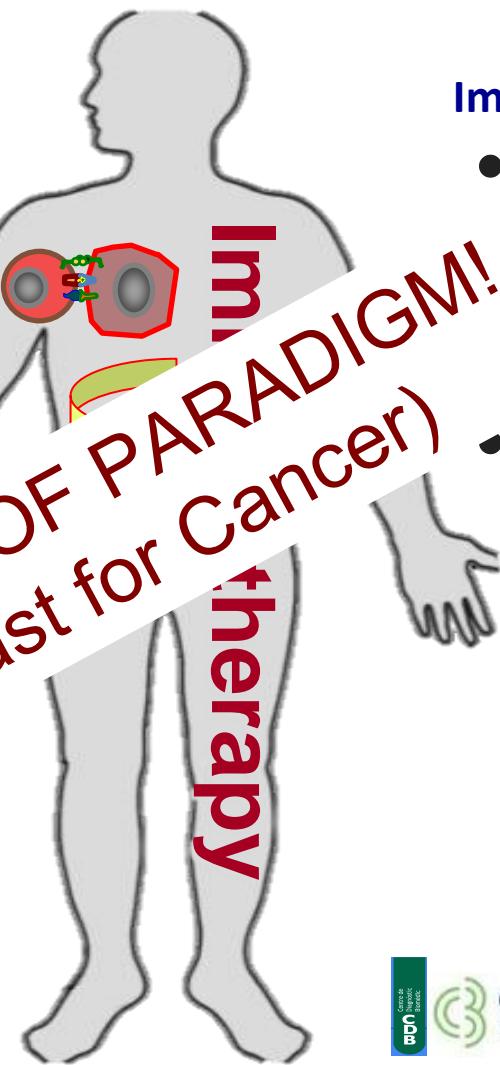
Co-Responsible of production of academic CART product (ARI-0001, ARI002 & other ATMPs) in patients with B-cell malignancies (CART19-BE-01 & CARTBCMA-HCB-01 trials) (including some companies as Immuneel, Cocoon or Gyala) + Hospital Exemption by AEMPS ... but **no-personal (economic) profit** from it.



Physical treatments: RTX,

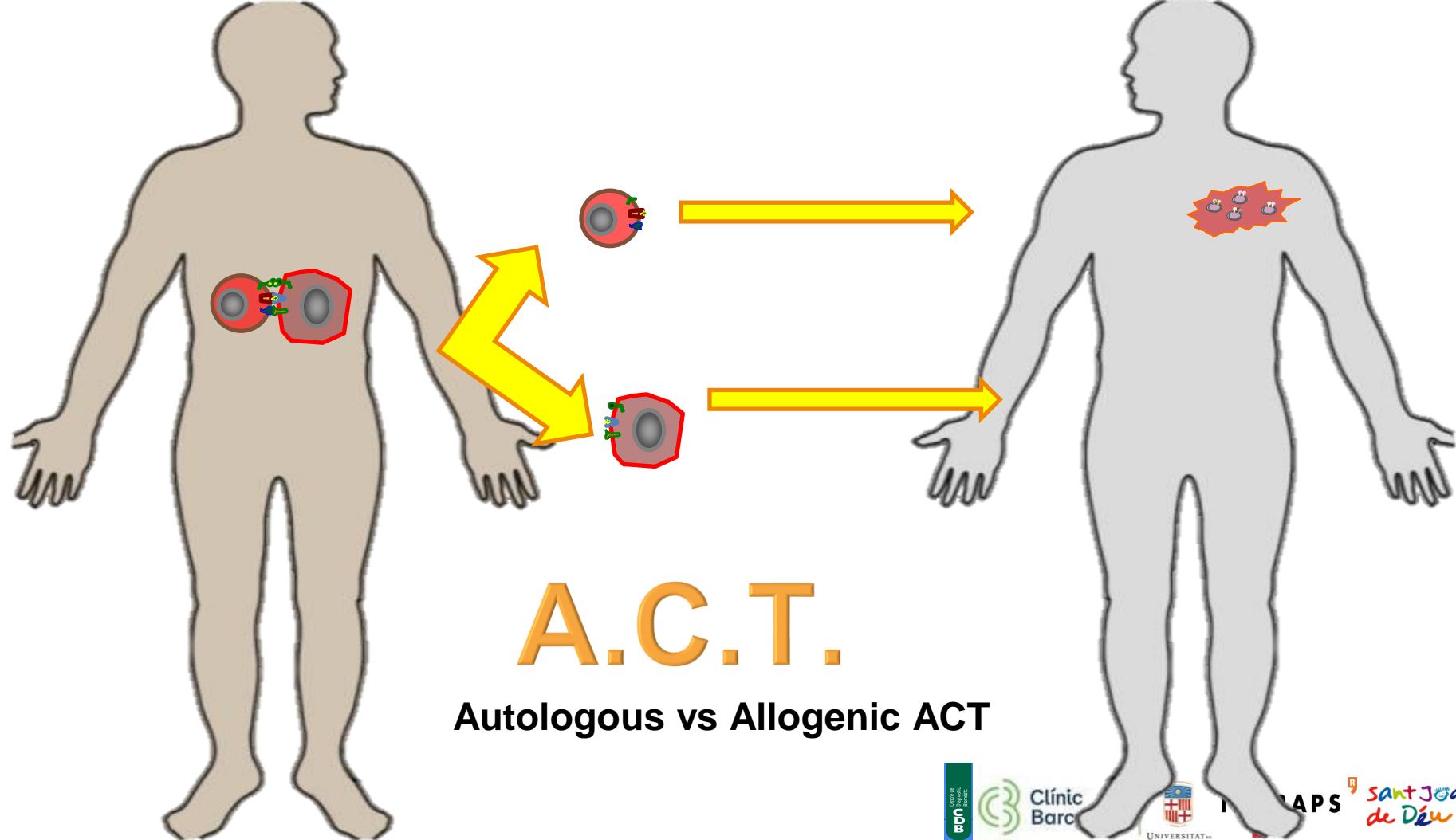


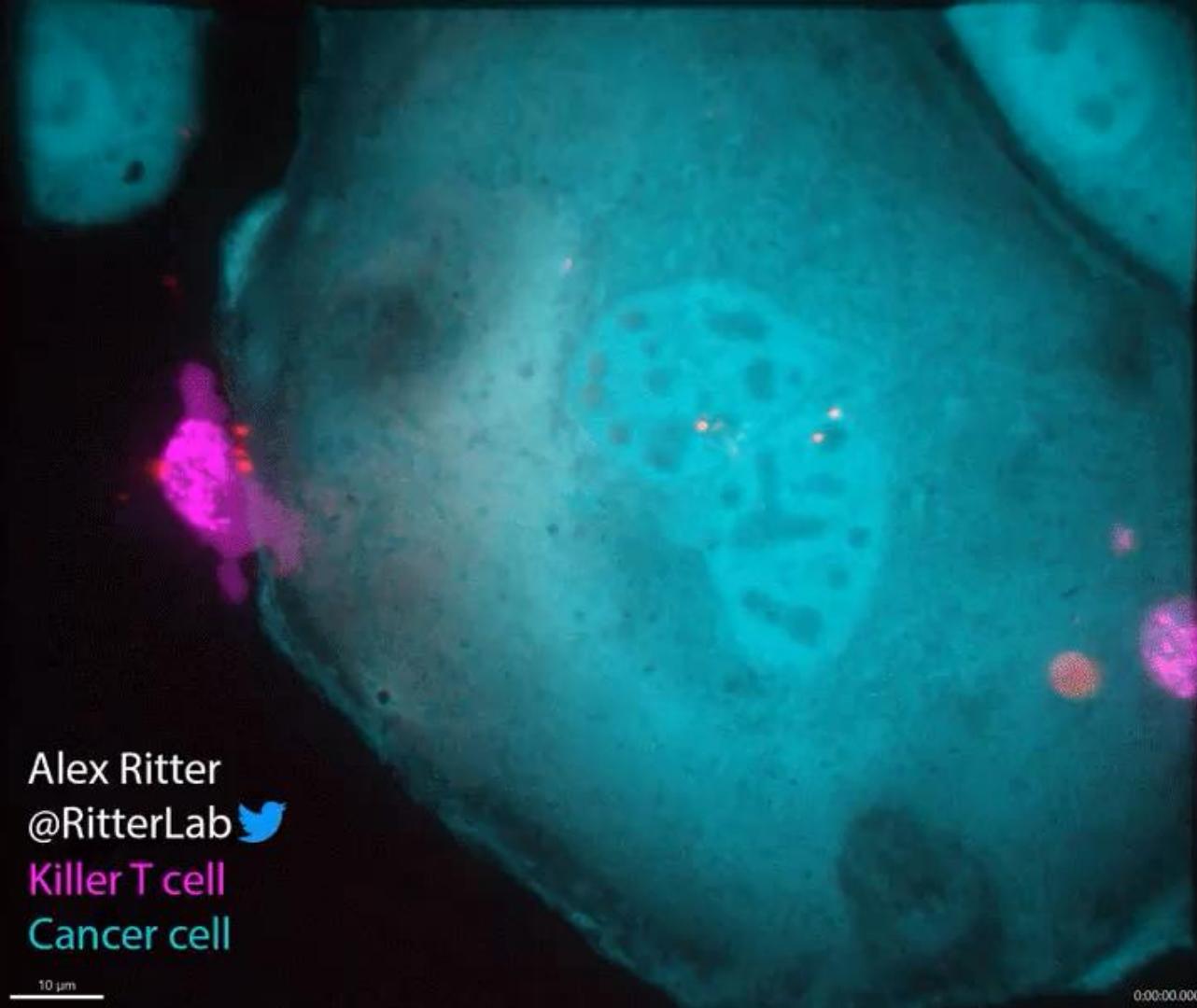
CHANGE OF PARADIGM!
(at least for Cancer)



Immune System

- Internal (we already have it). Continually effective (from minor infections).
- Specific – target-directed





Alex Ritter
@RitterLab 

Killer T cell
Cancer cell

10 μ m

0.00:00.000

ANTITUMORAL IMMUNOTHERAPY

Antibodies
(including Check-point
inhibitors)

SURGE

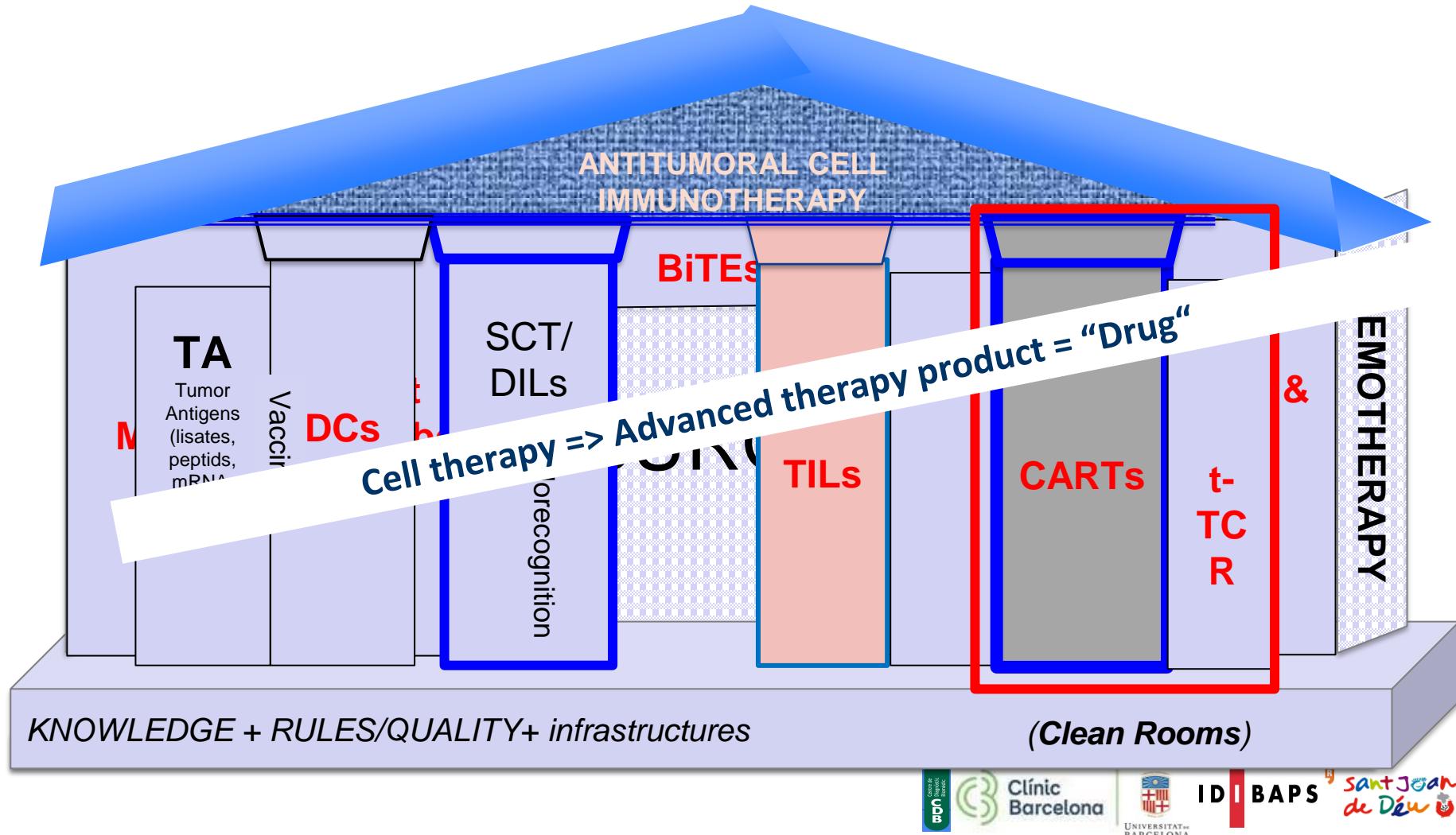
Cell & Gene
Immunotherapy
(including vaccines,
virotherapy, ...)

CHEMOTHERAPY

KNOWLEDGE + RULES/QUALITY+ *infrastructures*



Figure by author

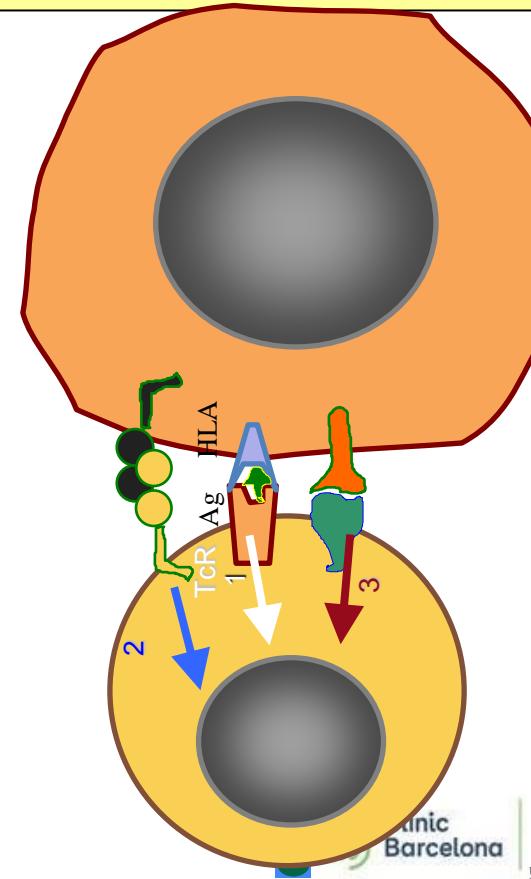


T-cell Cytotoxicity

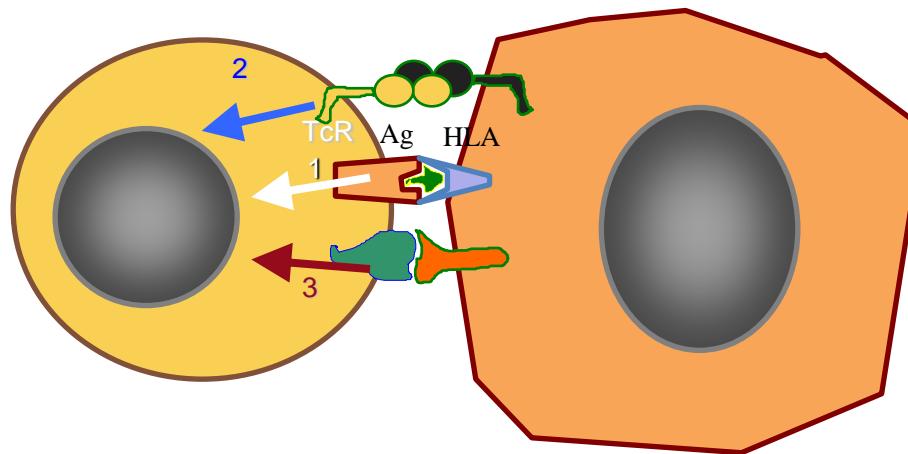
Cytotoxic T-Lymphocyte Killing Target

© James A. Sullivan
Quill Graphics
Charlottesville, VA USA

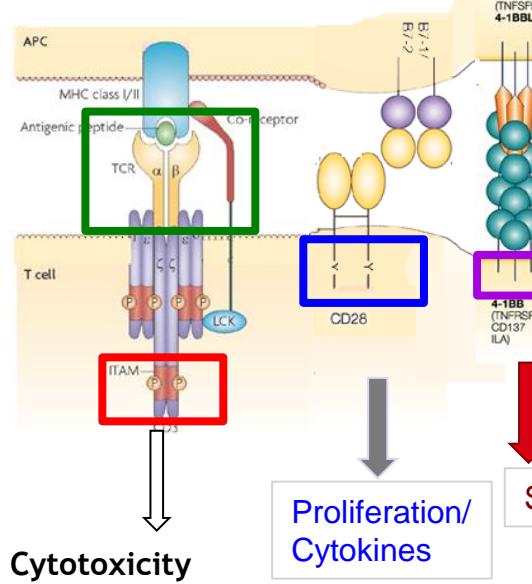
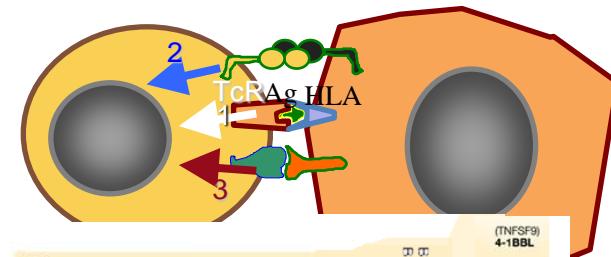
T-cell Cyotoxicity: TA recognition & more



T-cell Cyotoxicity: TA recognition & more



T-cell Cyotoxicity: TA recognition & more

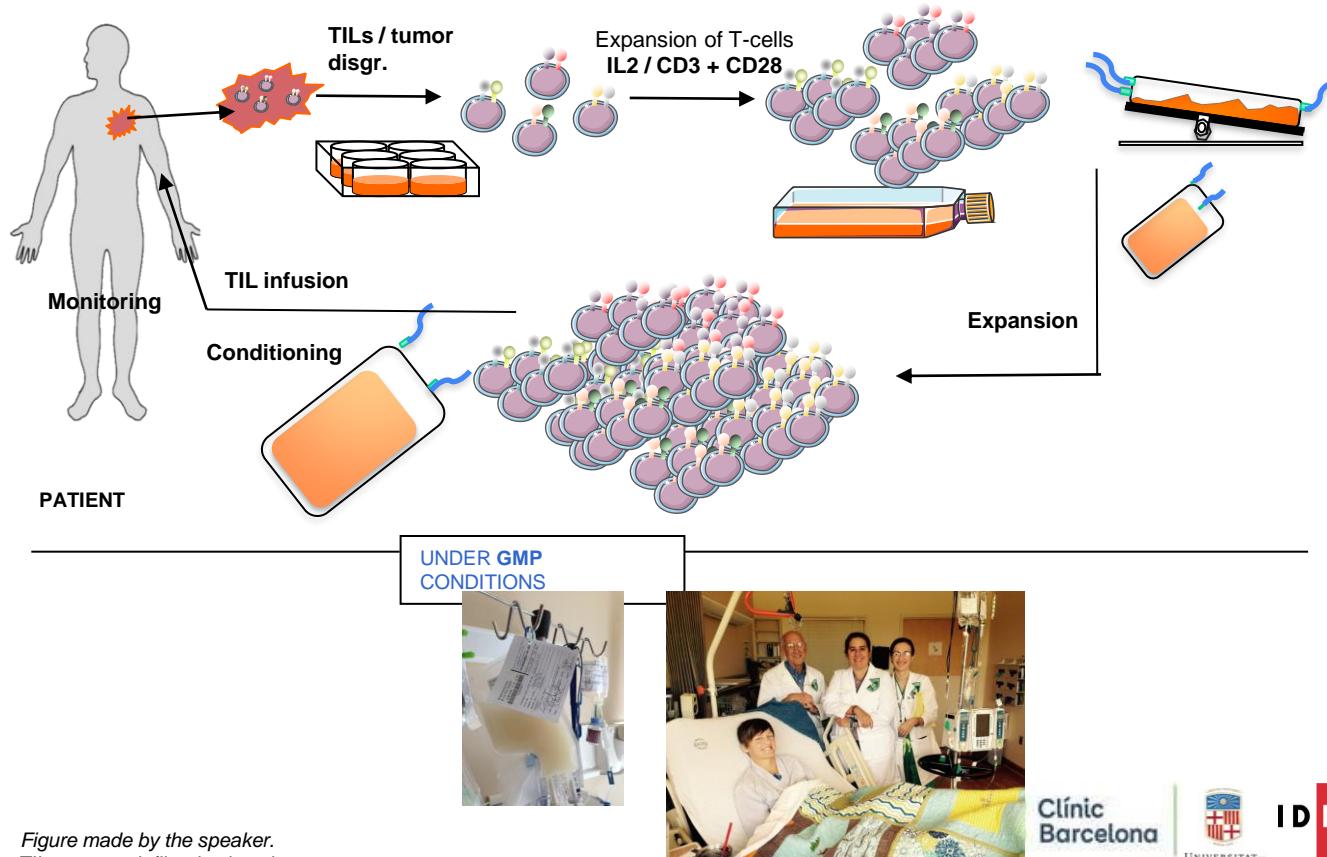


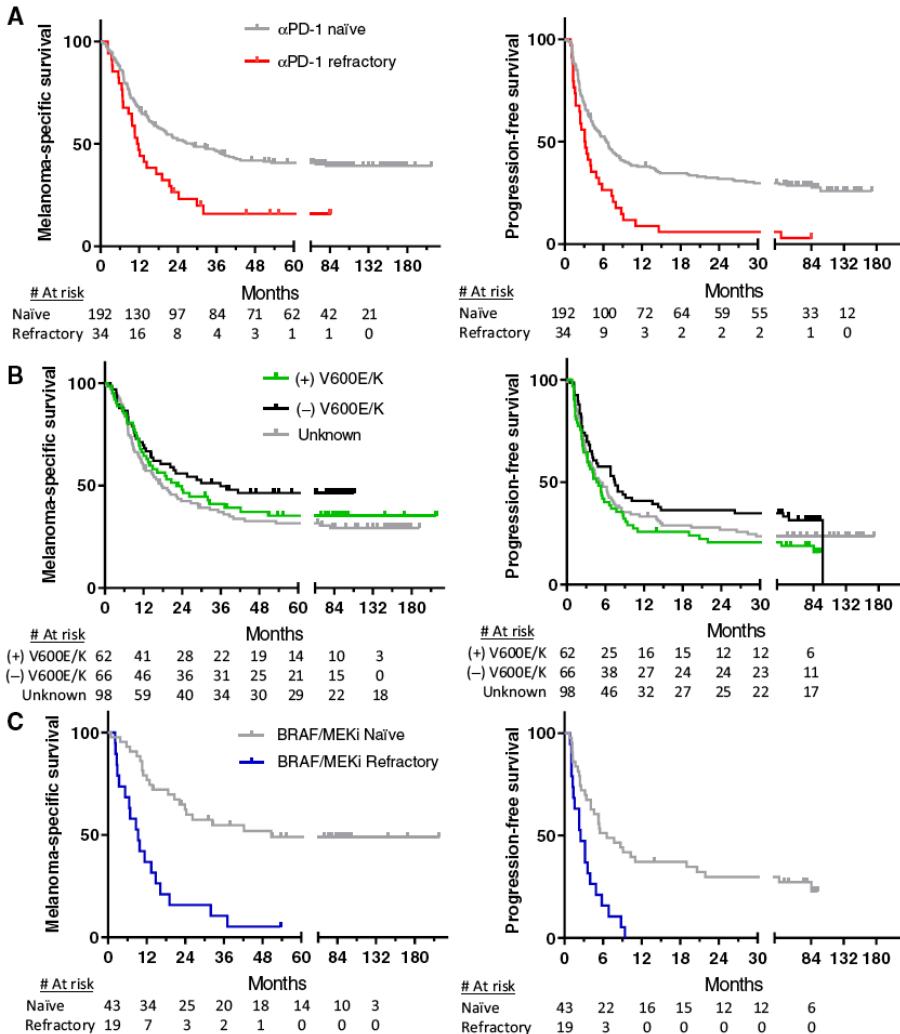
Clínica
Barcelona



IDI BAPS
Sant Joan
de Déu

TILs





Impact of Prior Treatment on the Efficacy of Adoptive Transfer of Tumor-Infiltrating Lymphocytes in Patients with Metastatic Melanoma

Seitter SJ et al.
Clin Cancer Res
2021;27:5289–98

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

DECEMBER 8, 2022

VOL. 387 NO. 23

Tumor-Infiltrating Lymphocyte Therapy or Ipilimumab in Advanced Melanoma

M.W. Rohaan, T.H. Borch, J.H. van den Berg, Ö. Met, R. Kessels, M.H. Geukes Foppen, J. Stoltenborg Granhøj, B. Nuijen, C. Nijenhuis, I. Jedema, M. van Zon, S. Scheij, J.H. Beijnen, M. Hansen, C. Voermans, I.M. Noringriis, T.J. Monberg, R.B. Holmstroem, L.D.V. Wever, M. van Dijk, L.G. Grijpink-Ongering, L.H.M. Valkenet, A. Torres Acosta, M. Karger, J.S.W. Borgers, R.M.T. ten Ham, V.P. Retel, W.H. van Harten, F. Lalezari, H. van Tinteren, A.A.M. van der Veldt, G.A.P. Hospers, M.A.M. Stevense-den Boer, K.P.M. Suijkerbuijk, M.J.B. Aarts, D. Piersma, A.J.M. van den Eertwegh, J.-W.B. de Groot, G. Vreugdenhil, E. Kapiteijn, M.J. Boers-Sonderen, W.E. Fiets, F.W.P.J. van den Berkmortel, E. Ellebaek, L.R. Hölmich, A.C.J. van Akkooi, W.J. van Houdt, M.W.J.M. Wouters, J.V. van Thienen, C.U. Blank, A. Meerveld-Eggink, S. Klobuch, S. Wilgenhof, T.N. Schumacher, M. Donia, I.M. Svane, and J.B.A.G. Haanen

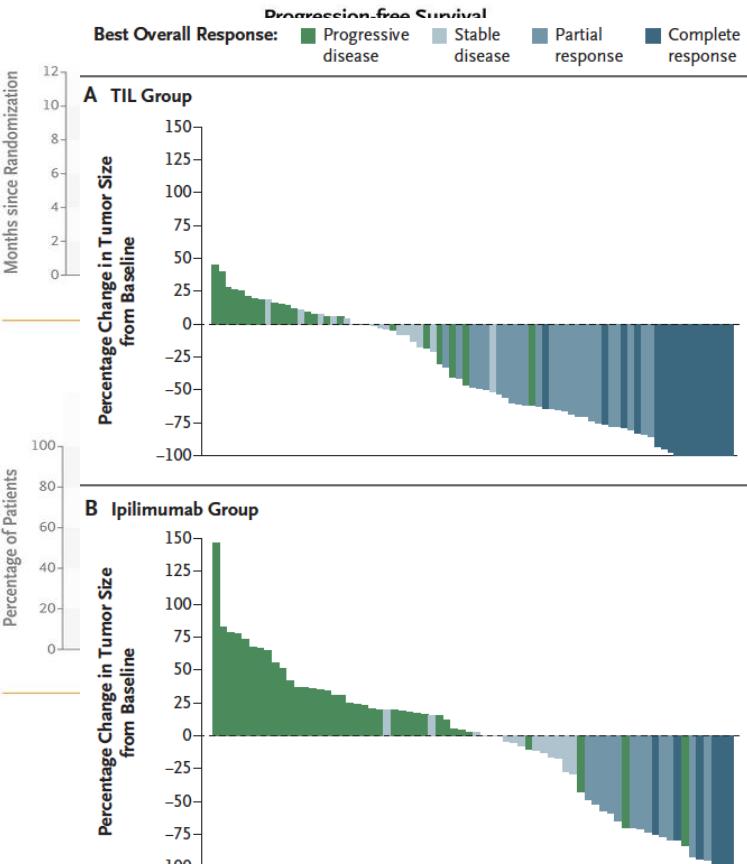
EDITORIALS

TIL Therapy Entering the Mainstream



George Coukos, M.D., Ph.D.

“... response in **49% of the patients** with melanoma who received **TILs** (most of whom had previously received anti-PD-1 therapy), as compared with a response in **21%** of the patients who received **ipilimumab**, findings that show the clear superiority of **TIL therapy over ... (CTLA-4) blockade** as second-line treatment. Both multicenter investigations show that TIL therapy can no longer be considered a “boutique” treatment and is entering the mainstream.



ACT → durable responses in solid tumors

	N	ORR	DoR months
MELANOMA (Rosenberg; CCR, 2011)	4		82+, 81+, 79+, 78+, 64+
MELANOMA (Rosenberg; CCR, 2011)	2		68+, 64+, 60+, 57+, 54+
MELANOMA (Rosenberg; CCR, 2011)	2		48+, 45+, 44+, 44+, 39+, 38+, 37+, 19+, 20, 22
MELANOMA (Besser; CCR, 2010)	2		20+, 4+
MELANOMA (Ellebaek; JTM, 2012)	6	33%	30+, 10+
UVEAL MELANOMA (Chandranl; Lancet Oncol, 2017)	2	35%	21+
	0		

18% with complete response (25/139)

18 pts with maintained response after 2 years

	N	ORR	DoR months
Unselected ACT			
OVARIAN CANCER (Pedersen; Oncolimmunology, 2018)	6	0%	NA
Selective ACT			
CHOLANGIOCA (Tran; Science, 2014)	1	PR	35
COLORECTAL (Tran; NEJM, 2016)	1	PR	9
BREAST CANCER (Zacharakis; Nature med, 2018)	1	CR	22+



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de BARCELONA



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de Déu



ASUNTO: Respuesta a Condiciones en la Resolución de Autorización
2020-003638-19

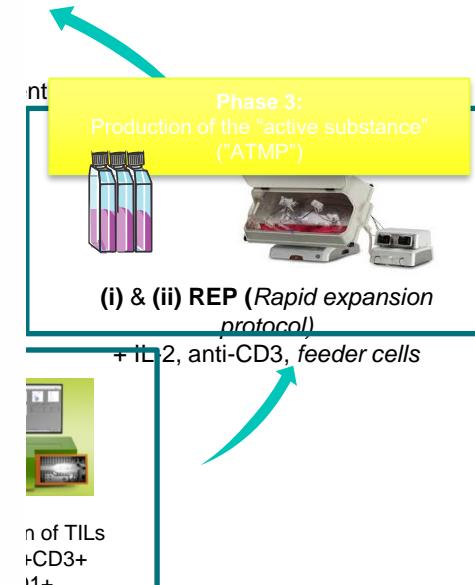
DESTINATARIO: CTU CLINIC
Villarroel 170
08036 Barcelona

PROMOTOR: Fundació Clínic per a la Recerca Biomèdica
Rosselló 149-153
08036 Barcelona

En relación con las respuestas recibidas en fecha 11 de Julio de 2022 para las condiciones de la Resolución de Autorización del ensayo clínico titulado:

Tratamiento de cáncer de mama triple negativo avanzado o metastásico con terapia adoptiva de linfocitos infiltrantes de tumor PD1 positivo.

Tras evaluar la respuesta a las condiciones de autorización de este ensayo, la AEMPS comunica que **está conforme con las mismas**.

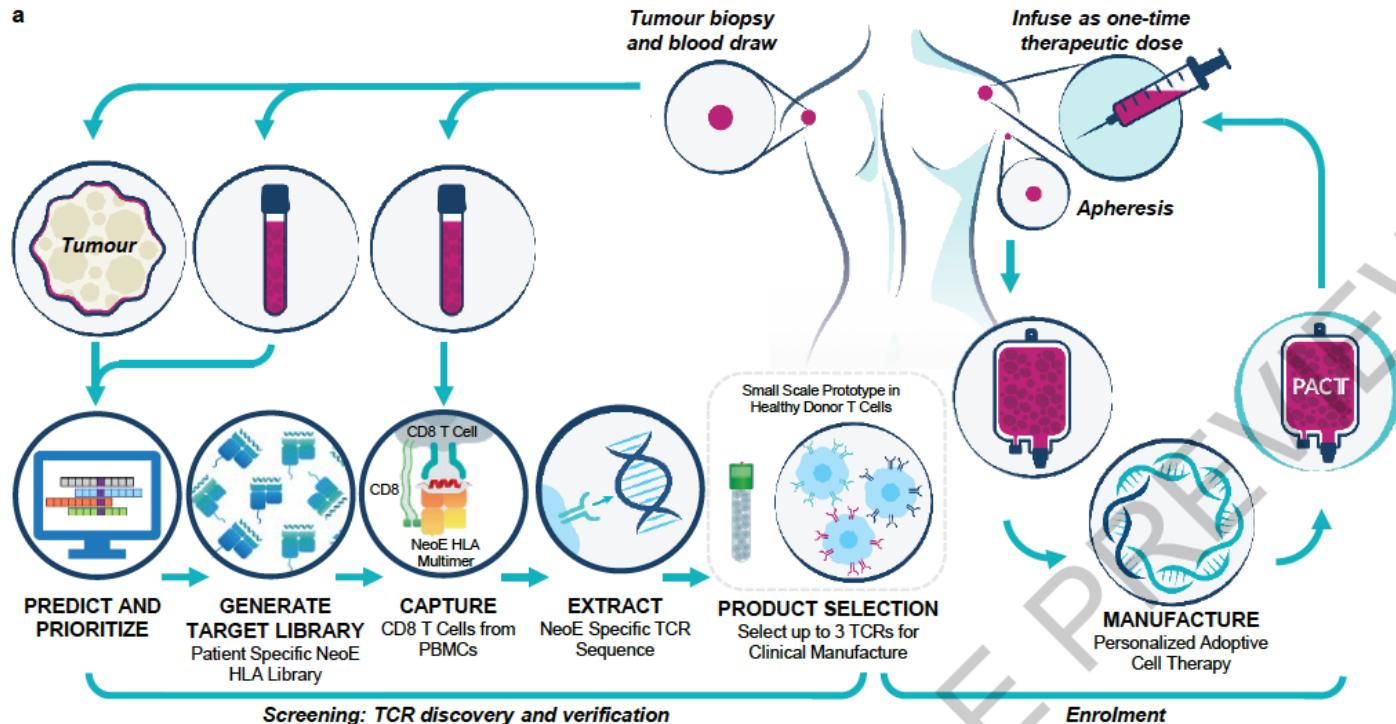


JEFE DE DEPARTAMENTO DE MEDICAMENTOS DE USO HUMANO

agencia española de
medicamentos y
productos sanitarios
Cesar Hernández García

Accelerated Article Preview

Non-viral precision T cell receptor replacement for personalized cell therapy



RESEARCH SUMMARY

Tumor-Infiltrating Lymphocyte Therapy or Ipilimumab in Advanced Melanoma

Rohaan MW et al. DOI: 10.1056/NEJMoa2210233

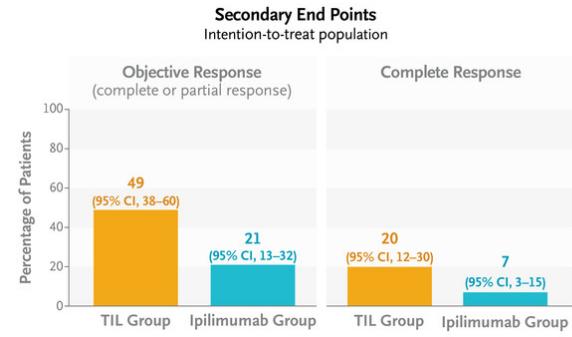
Progression-free Survival

HR for disease progression or death, 0.50
(95% CI, 0.35–0.72); $P < 0.001$



Secondary End Points

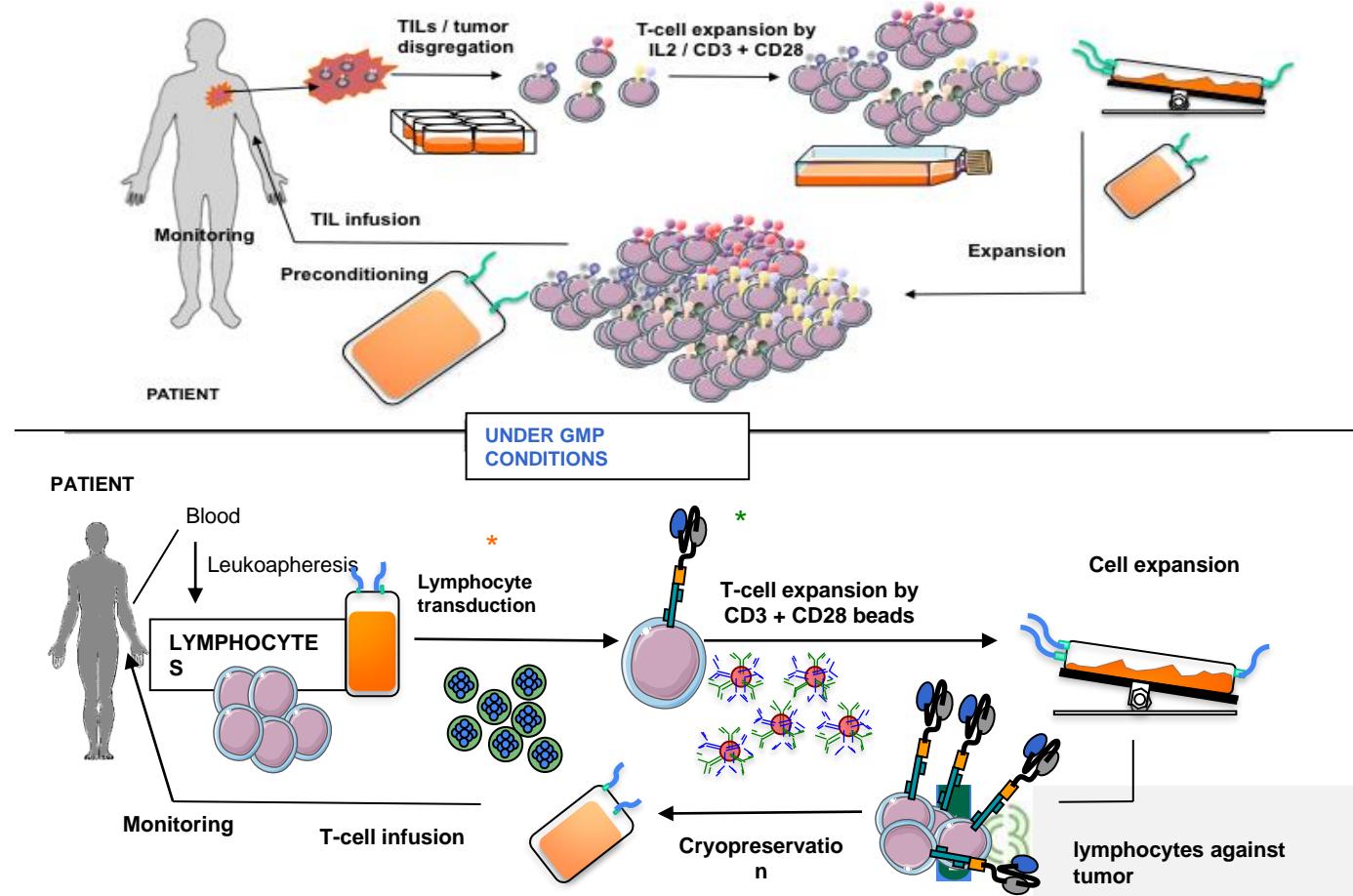
Intention-to-treat population

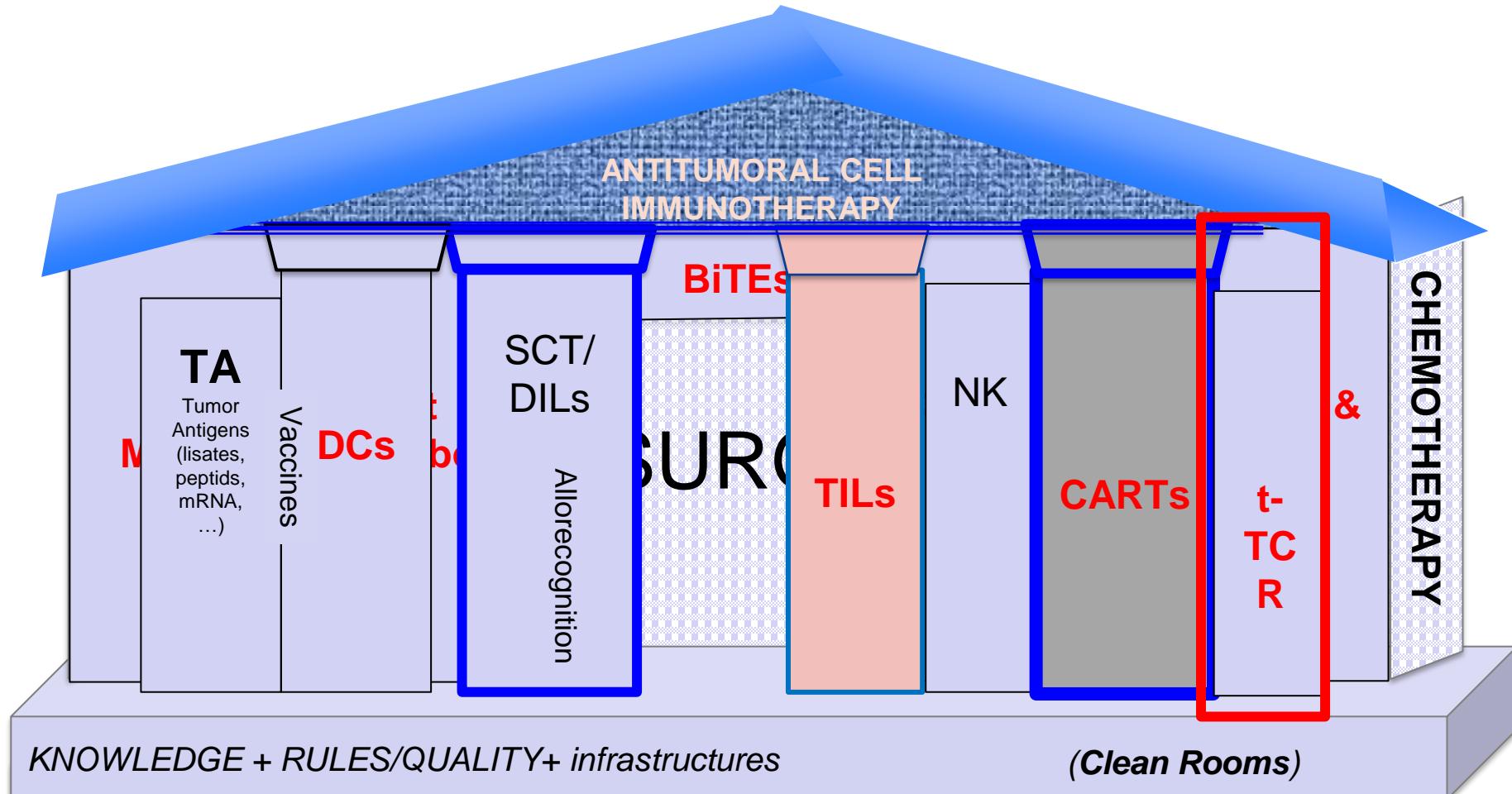


CONCLUSIONS

In patients with advanced melanoma, progression-free survival was longer among those who received adoptive cell therapy with TILs than among those who received ipilimumab immunotherapy.

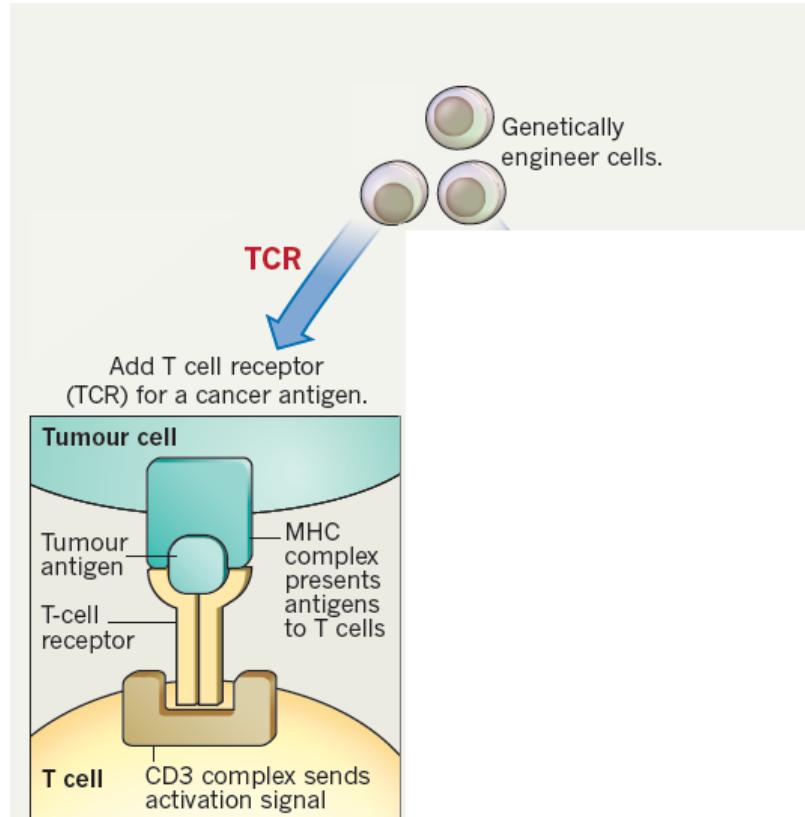
From TILs to T-cell modified therapy

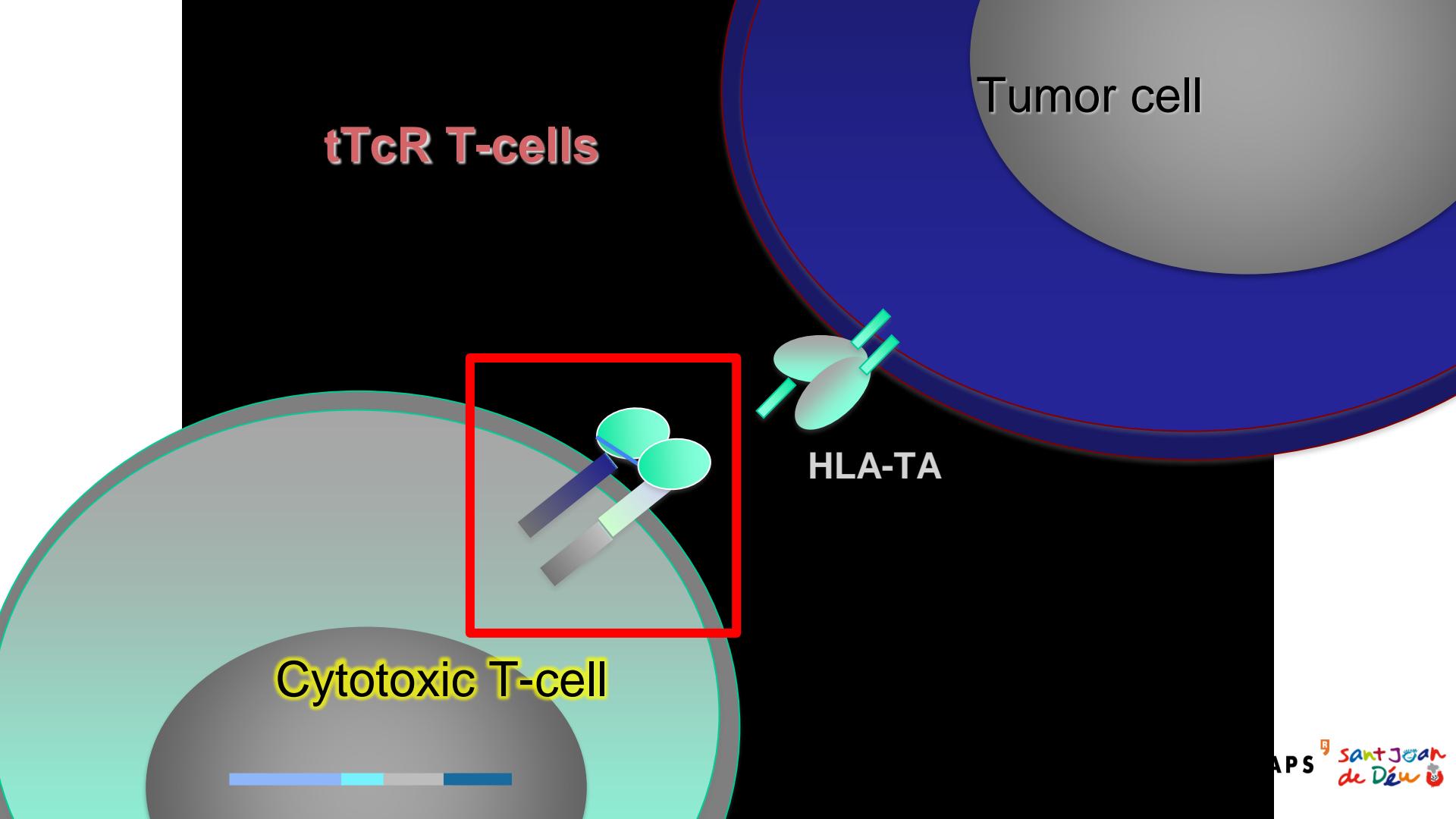




Ex vivo modification of T-cell

Humphries
C, Nature
504, S13-
S15 2013

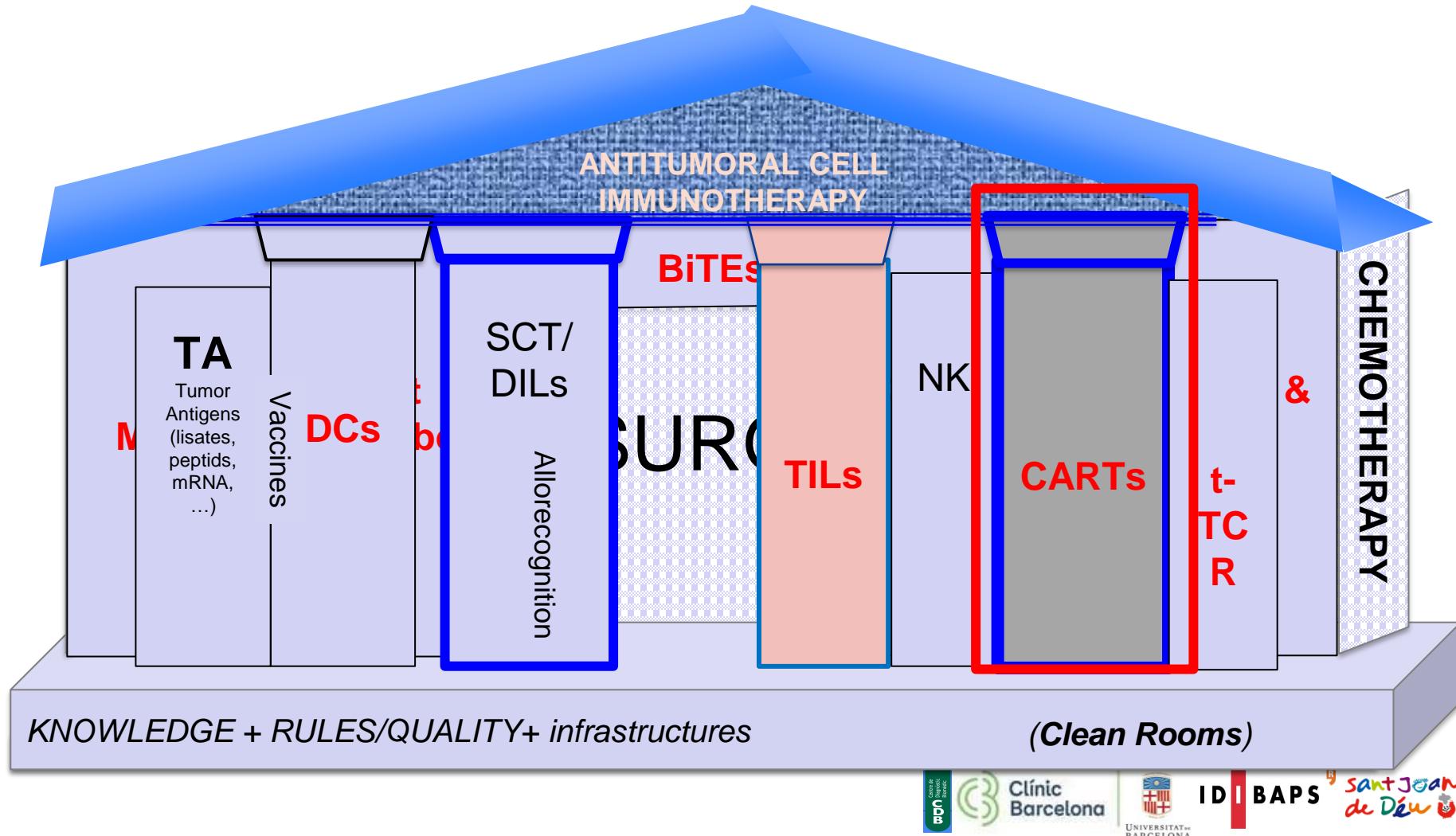




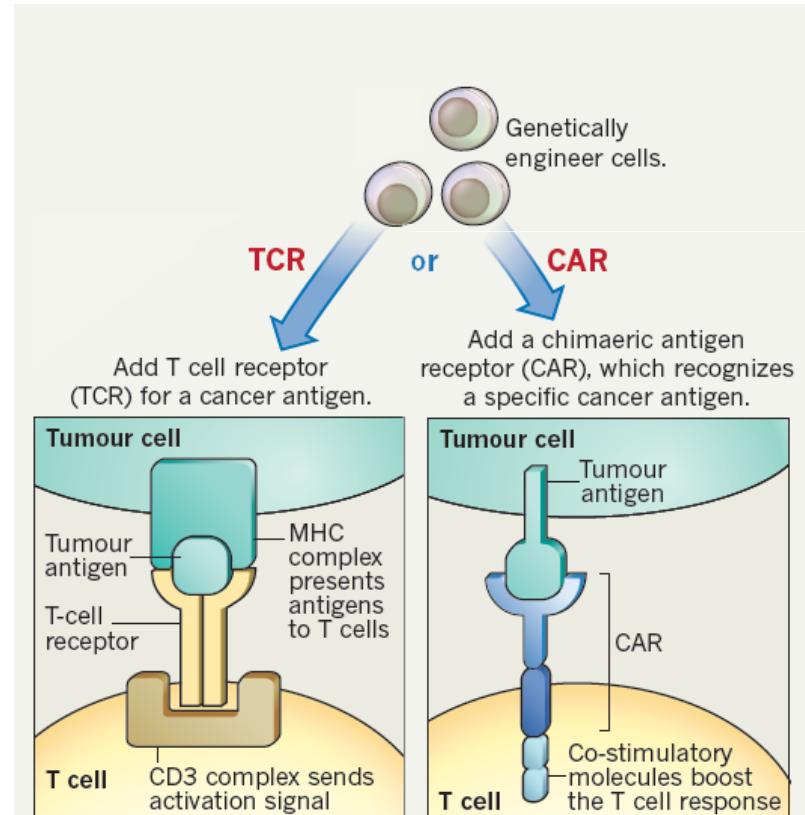
Target	Trial number	Study period (Status)	Patient no (est.)	Vector/mode	HLA allele	Cancer targeted	
MART-1	NCT00509288	2007-2011 (C)	24	Retroviral vector	HLA-A *0201	Metastatic cutaneous melanoma ²	
	NCT00612222	2008-2011 (T)	4	Retroviral vector + ALVAC vaccine	HLA-A *0201	Metastatic cutaneous melanoma	
	NCT00910650	2009-2019 (C)	14	+ dendritic cell vaccine	HLA-A *0201	Metastatic cutaneous melanoma ³	
	NCT02654821	2012-2019 (A, nr)	12 (25)	Retroviral vector	HLA-A *0201	Metastatic cutaneous and uveal melanoma	
MART-1 gp 100	NCT00923195	2008-2011 (C)	4 (85)	Retroviral vector + peptide vaccine	HLA-A *0201	Metastatic cutaneous melanoma ⁴	
	NCT00610311	2008-2011 (T)	3	+ ALVAC vaccine murine TCR	HLA-A *0201	Metastatic cutaneous melanoma	
	NCT00509496	2007-2011 (T)	21	Retroviral vector	HLA-A *0201	Metastatic cutaneous melanoma	
NY-ESO-1	NCT00670748	2008-2016 (T)	45	Retroviral vector	HLA-A *0201	Metastatic cancers, melanoma/RCC and others ⁵	
	NCT01457131	2011-2013 (T)	2	Retroviral vector w/inducible IL-12	HLA-A *0201	Metastatic cancers, melanoma and others	
	NCT01350401	2011-2016 (T)	4	Lentiviral vector enhanced TCR	HLA-A *0201	Metastatic, cutaneous melanoma	
	NCT01967823	2013-2020 (C)	11	Retroviral vector murine TCR	HLA-A *0201	Metastatic cancers, melanoma and others	
	NCT02062359	2014-2016 (T)	2	Retroviral vector CD62L+ T cells	HLA-A *0201	Metastatic cutaneous melanoma	
	NCT02366546	2015-2018 (A, nr)	9 ¹	Unknown	HLA-A *0201 HLA-A*02:06	Metastatic cancers, melanoma and others	
	NCT02457650	2015-2019 (R)	36 ¹	Unknown	HLA-A *0201	NY-ESO-1 + malignancies (children and adult)	
	NCT02869217	2016-2020 (A, nr)	22 ¹	Unknown	HLA-A *02:01 HLA-A*02:06	Metastatic cancers, melanoma and others	
	NCT03638206	2018-2023 (R)	73 ¹ (incl. CAR-T trial)	Unknown	HLA-A *02:01	Metastatic cancers, melanoma and others incl. multiple myeloma	
	NCT03399448	2018-2033 (A, nr)	3 ¹	Lentiviral vector CRISPR TCRendo and PD-1	HLA-A *02:01	Metastatic cancers, melanoma and others	
MAGE	A3/12	NCT01273181	2010-2012 (T)	9 (97)	Retroviral vector	HLA-A *0201	Metastatic cancers, melanoma and RCC ⁶
	A3	NCT02153905	2014-2018 (T)	3 (102)	Retroviral vector	HLA-A *01	Metastatic cancers, melanoma and others
	A3	NCT021111850	2014-2023 (R)	17 ¹ (107)	Retroviral vector CD4 TCR	HLA-DP4	Metastatic cancers, melanoma and others ⁷
	A4	NCT01694472	2012-2016 (U)	15 ¹	Unknown	HLA-A *24:02	Metastatic cancers, melanoma and others
	A4	NCT03132922	2017-2020 (R)	42 ¹	Lentiviral vector	HLA-A *02	Metastatic cancers, melanoma and others
	A10	NCT02989064	2016-2019 (A, nr)	22 ¹	Lentiviral vector	HLA-A *02:01 HLA-A*02:06	Metastatic cancers, melanoma and others
	A1	NCT03441100	2019-2020 (R)	(16) ¹	Viral vector IMA202	Unknown	Metastatic cancers, melanoma and others
	PRAME	NCT02743611	2017-2019 (A, nr)	28 (36)	Rimiducid-inducible safety switch	HLA-A *02:01	Metastatic uveal melanoma, relapsed AML and MDS
		NCT03686124	2019-2021 (R)	(16)	Viral vector IMA203	Unknown	Metastatic cancers, melanoma and others
p53	NCT00393029	2006-2008 (C)	12	Retroviral vector	HLA-A *02:01	Metastatic cancers, melanoma and others	
	NCT00704938	2008-2009 (T)	3 (82)	+dendritic cell vaccine	HLA-A *0201	Metastatic cancer, melanoma/RCC and others	
Tyrosinase	NCT01586403	2012-2028 (A, nr)	3(14) ¹	Retroviral vector	HLA-A *02	Metastatic melanoma ⁸	
Neoantigens	NCT03970382	2019 - (R)	(148)	CD8 and CD4 TCR ± nivolumab	Unknown	Metastatic cancers, melanoma and others	

Note: All clinical studies using TCR therapy against malignant melanoma registered on ClinicalTrials.gov. ¹No updated information on enrolment available; ²Ref 102; ³Ref 103; ⁴Ref 102; ⁵Ref 104; ⁶Ref 77; ⁷Ref 105; ⁸Ref 53.

Abbreviations: (A, nr), Active, not recruiting; (C), Completed; (R), Recruiting; (T), Terminated; (U), Unknown.

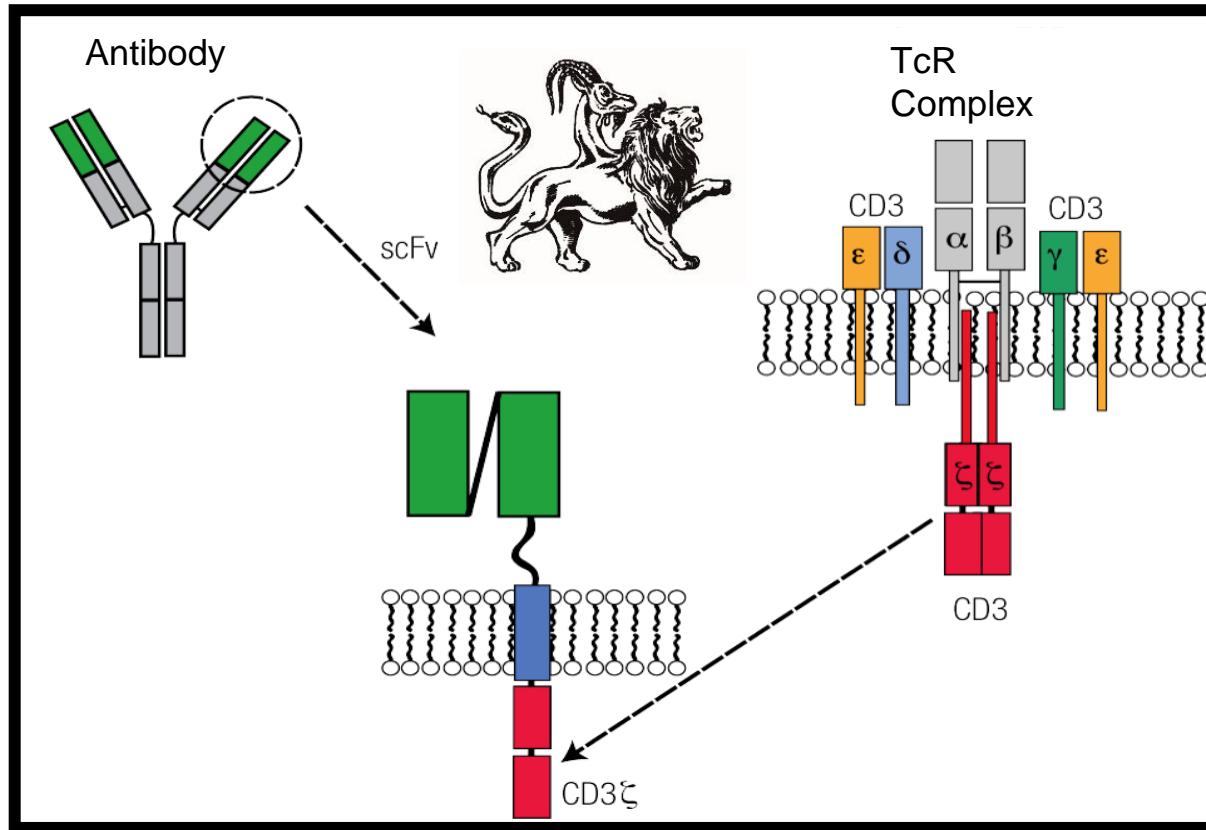


Ex vivo modification of T-cell



Humphries
C, Nature
504, S13-
S15 2013

CAR = Chimeric Antigen Receptor

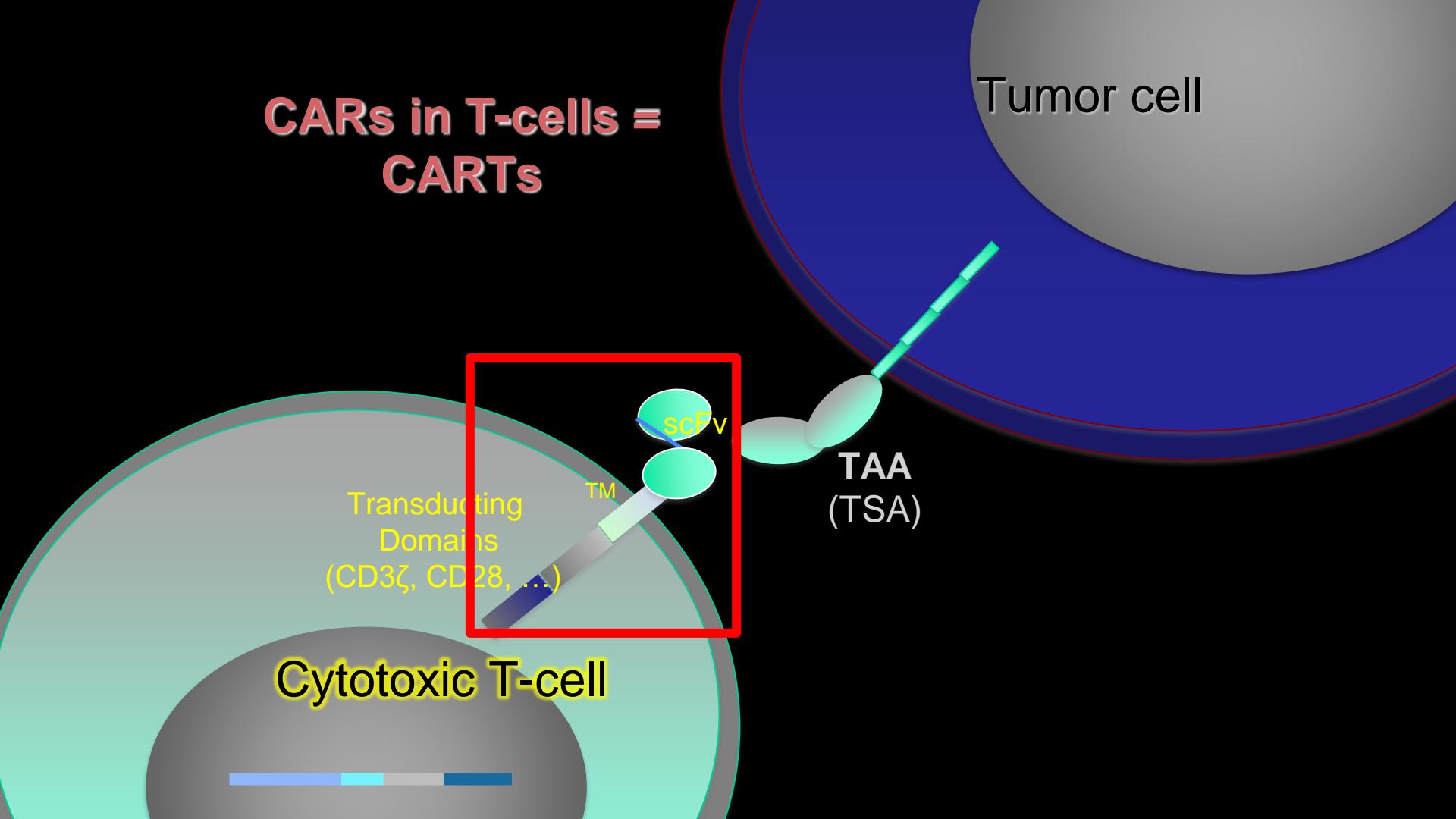


Sònia Guedán Carrió y Anna Boronat Barado

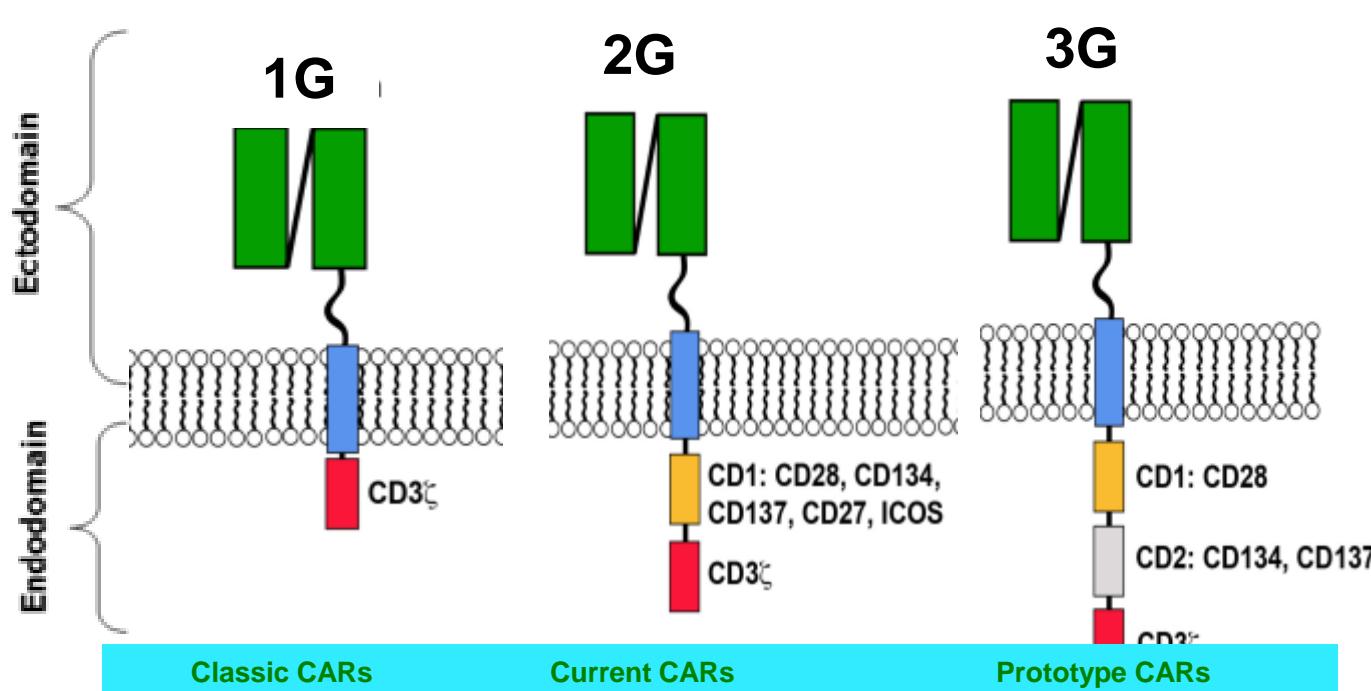
Chapter 6. Monografías SEI – Elsevier. "Inmunoterapia antitumoral con linfocitos genéticamente modificados (CAR): una realidad con futuro".



**CARs in T-cells =
CARTs**

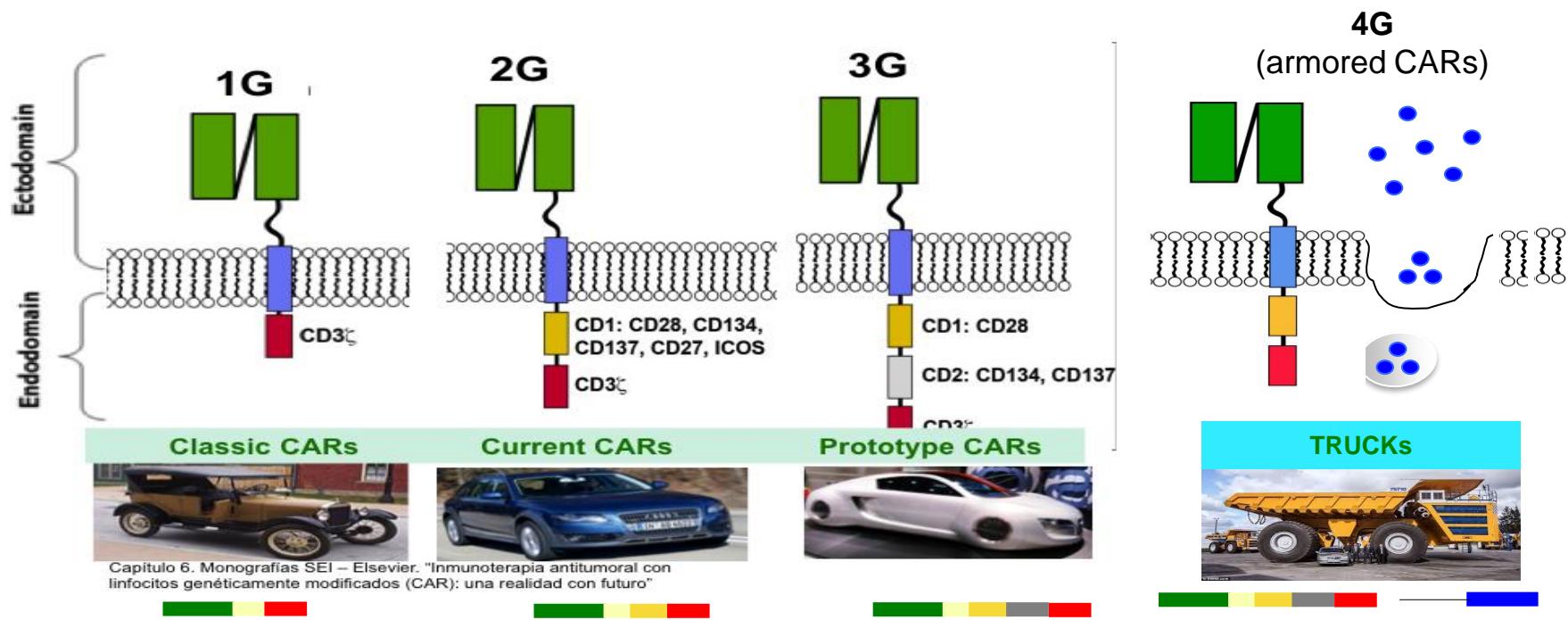


CAR evolution

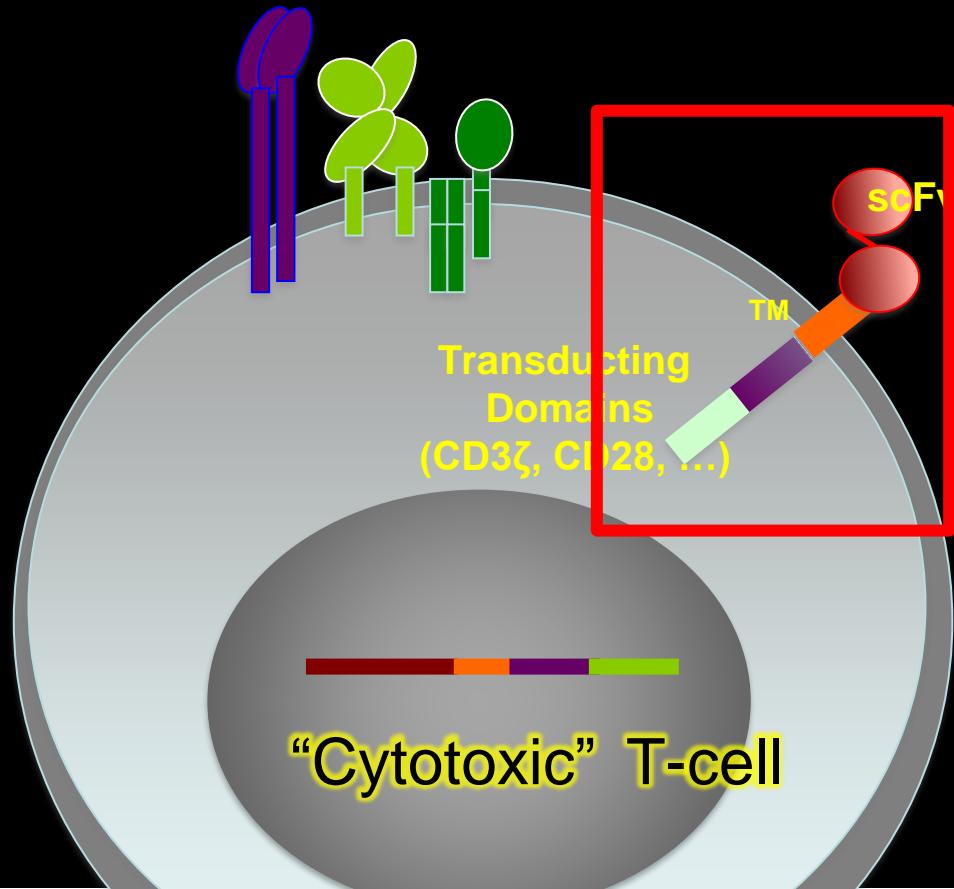


Capítulo 6. Monografías SEI – Elsevier. "Inmunoterapia antitumoral con linfocitos genéticamente modificados (CAR): una realidad con futuro".

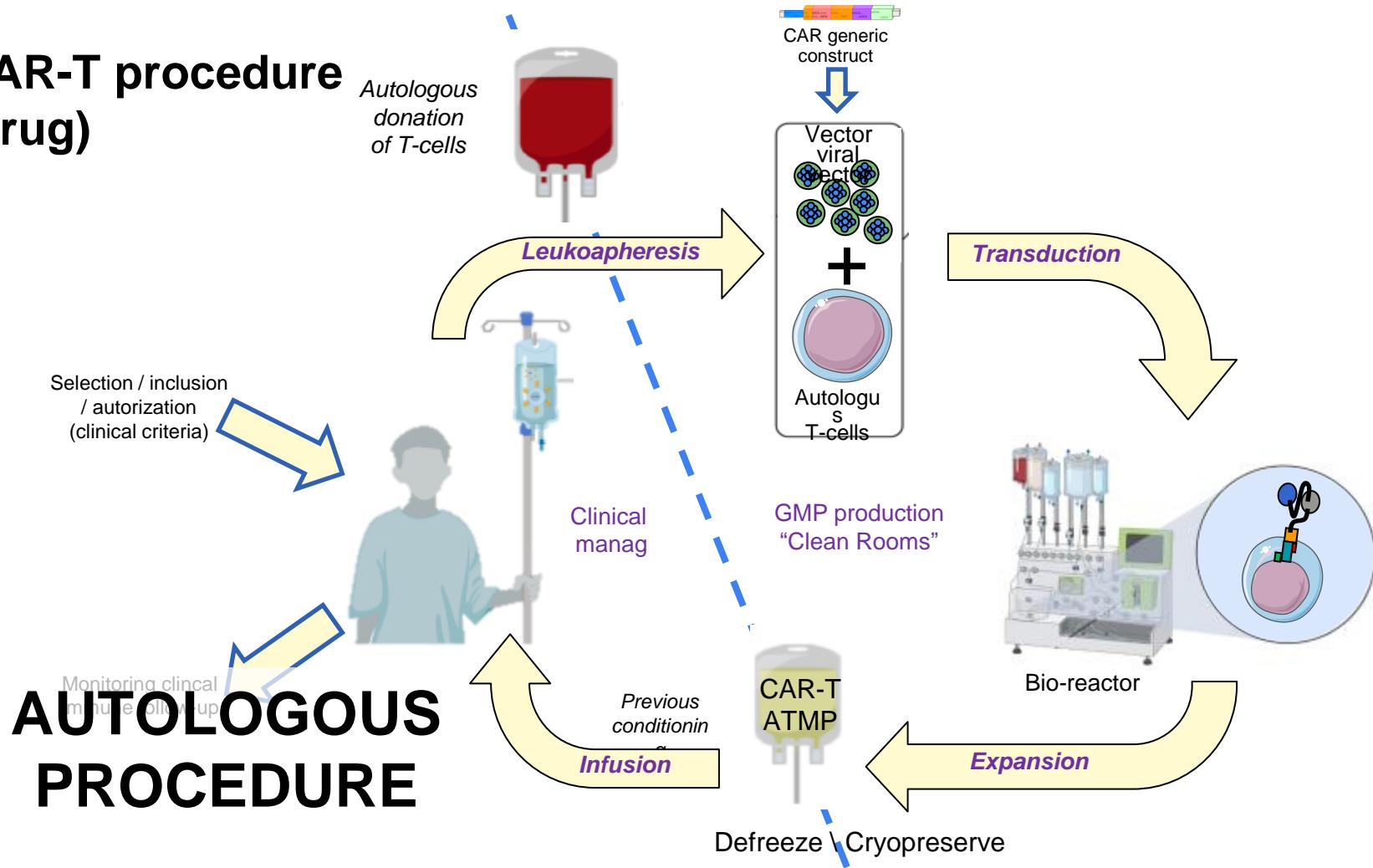
CAR evolution



CARs in T-cells = CARTs



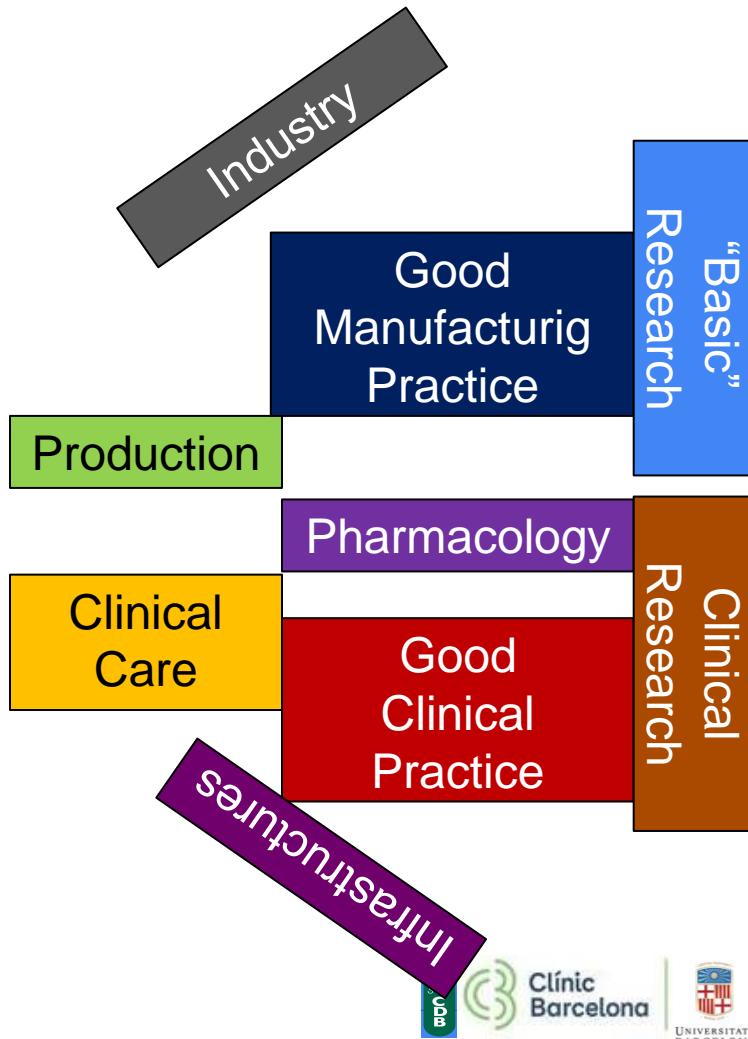
CAR-T procedure (drug)



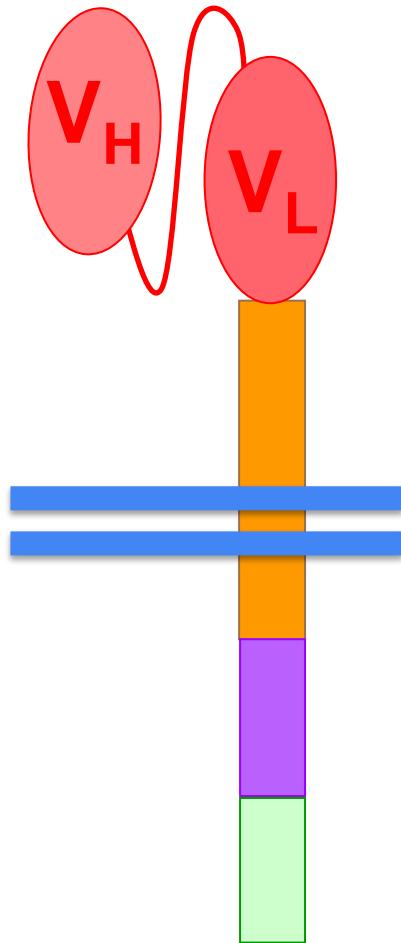
Healthcare



32



2-G CAR



scFv

= Tumor Antigen Recognition

Current CARs



hinge +
Transmembrane
(CD8a ... others)

CD137 / CD28 = 2nd signal - 3rd signal
(Costimulatory domain)

CD3ζ = 1st signal

(Signalling domain)



FDA / EMA CART19 / CART-BCMA approved:

Since August-October 2017 (FDA) / July 2018 (EMA) / July 2020 (FDA) / February 2022 (FDA)



Novartis ALL & DLBCL <25 y
USA: 475,000 \$ / patient)

Spain: 320 m€



Kite NHL DLBCL:
USA 373 m\$ / patient

Spain: 340 m€

Kite MBCL Lymphoma (FDA)



TECARTUS™
(brexucabtagene autoleucel) Suspen
for IV



CART-BCMA approved. 2022

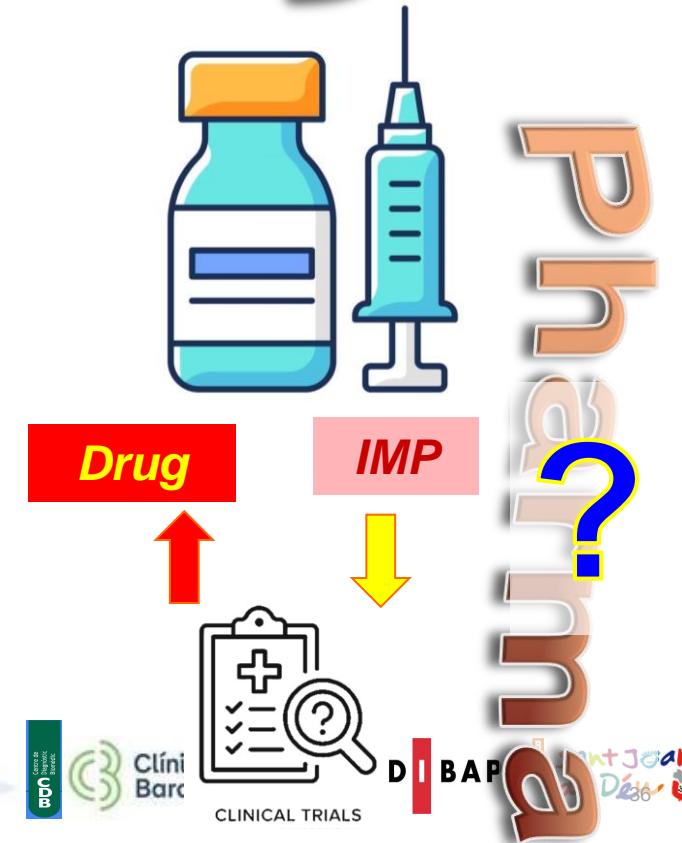


Biological principles of CAR T- cells.

CAR-T as antitumoral immunotherapy is based on 3 main factors

1. The product, engineered T-lymphocytes:
 - a) Cytotoxic T-cells (mainly CD8+).
 - b) Cytokine producing cells (mainly CD4+).
 - c) Capacity of Proliferation (both).
 - d) Capacity of cell survival and persistence (both).
2. Own Immune system (the main uncontroled parameter)
3. Clinical management of the process and the patient

KNOWLEDGE RESULTS Academy THESIS ? F HYPOTHESIS SOLUTION



Academic manufacture of CAR-T.

By now, all the CAR-T have been **initially developed from research teams**, so (by now) **industry** is “just” defining how to introduce **large-scale production** (accessibility?) and a perfect tracking of the process.

Academic manufacture is (by now) the base for introducing and improving new proposals.

But, (by now) industrial production and marketing of ATMPs is almost the **only way** to have products.

Success of CARs: Thousands of patients

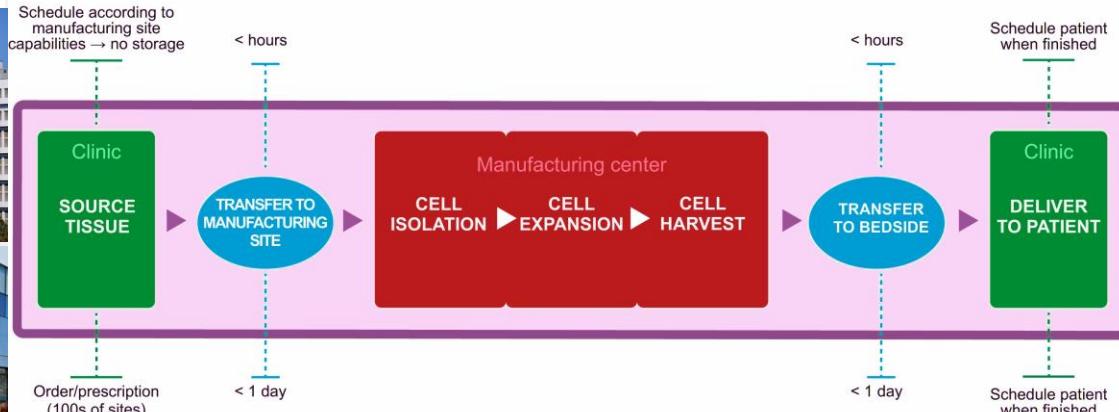
Commercial development



Academic development



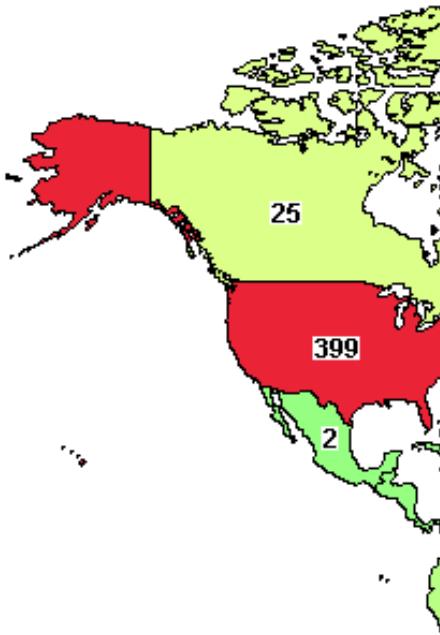
Schubert ML/ Schmid



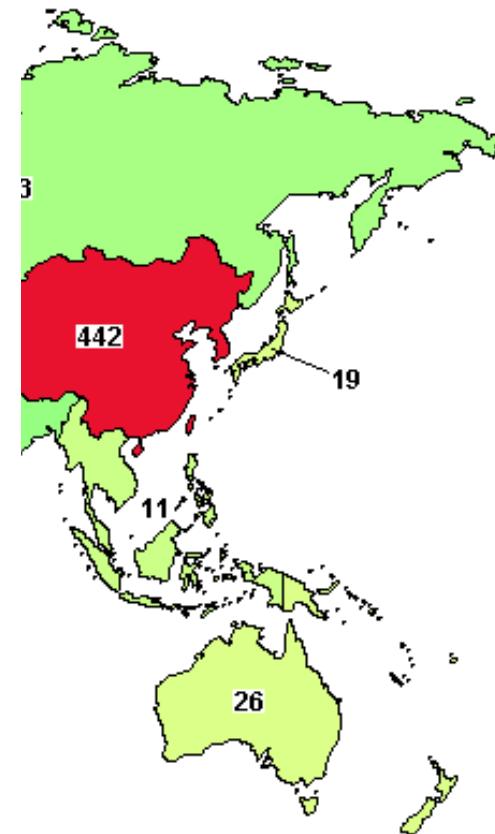
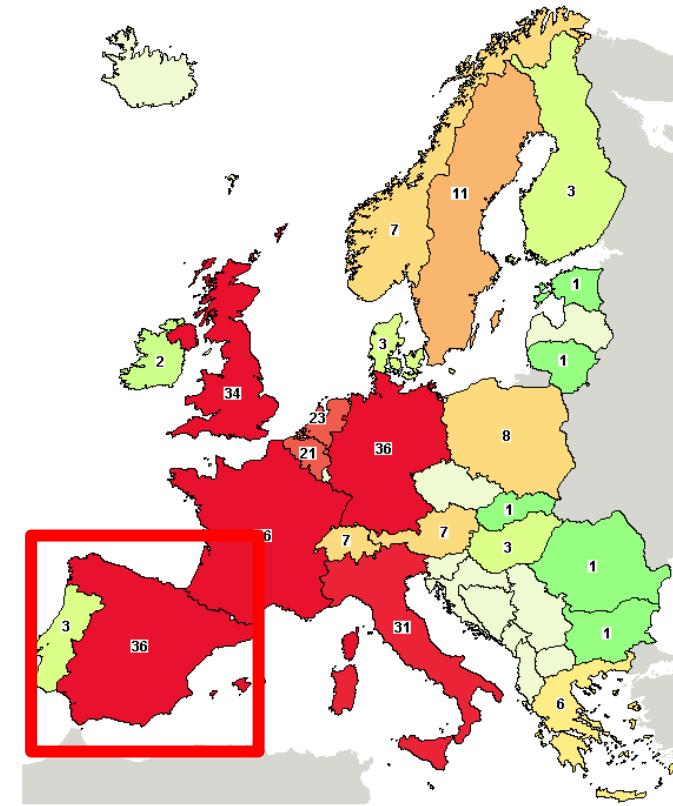
Commercial manufacturing - clinic and manufacturing center are physically disconnected



Clinical Trials “Chimeric Antigen Receptor = 968



September 2023



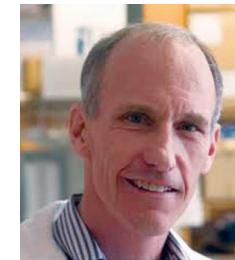
CART19 : August 2011, “seminal” article

The NEW ENGLAND JOURNAL of MEDICINE

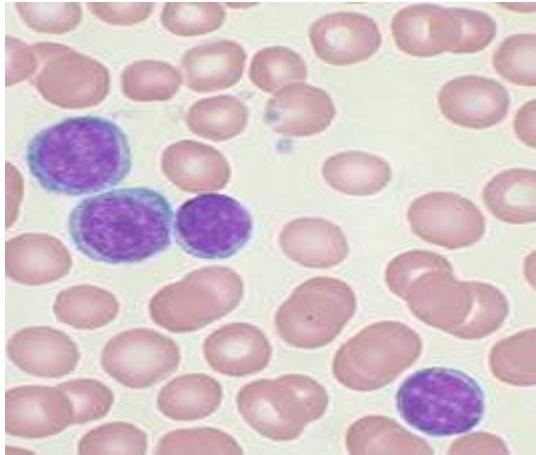
BRIEF REPORT

Chimeric Antigen Receptor–Modified T Cells in Chronic Lymphoid Leukemia

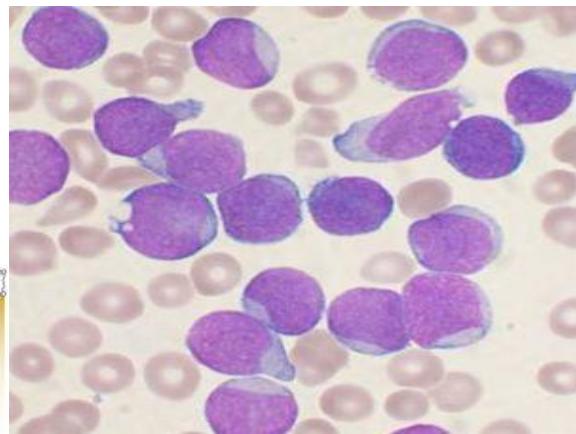
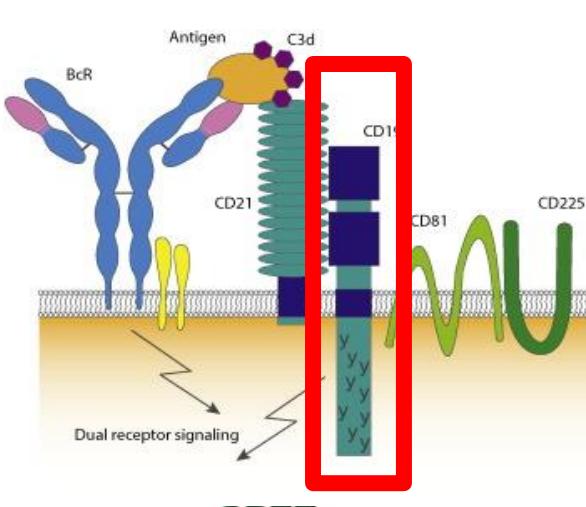
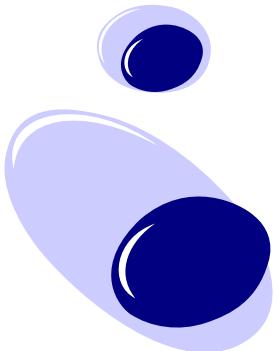
David L. Porter, M.D., Bruce L. Levine, Ph.D., Michael Kalos, Ph.D.,
Adam Bagg, M.D., and Carl H. June, M.D.



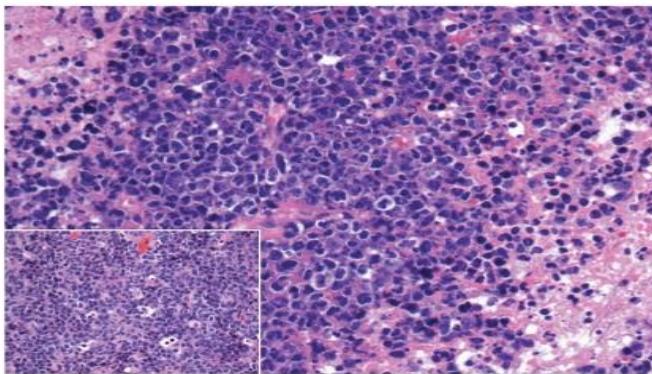
N ENGL J MED 365;8 NEJM.ORG AUGUST 25, 2011



Chronic Lymphocytic
Leukemia (CLL)



Acute Lymphoblastic
Leukemia (ALL)



Non-Hodgkin
Lymphoma (NHL)

Obituaries

Bill Ludwig, patient who helped pioneer cancer immunotherapy at Penn, dies at 75 of COVID-19

The South Jersey man beat end-stage cancer with a breakthrough immune therapy. But he couldn't beat the pandemic.

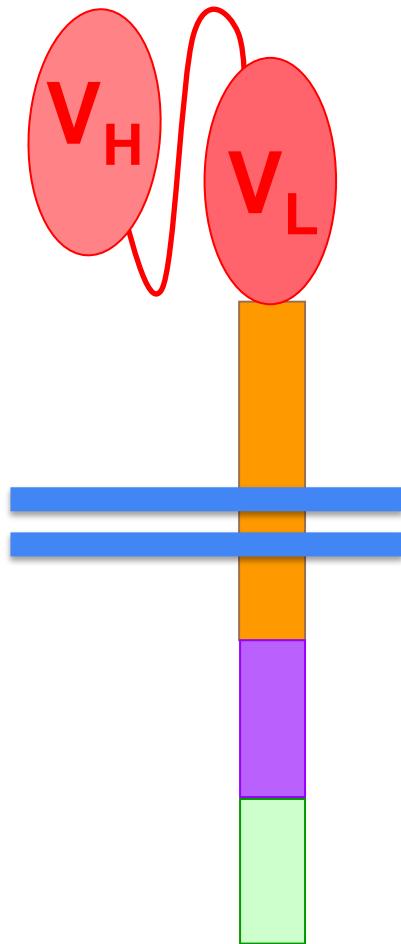


ADVERTISEMENT

Feb 17, 2021



2-G CAR



scFv

= Tumor Antigen Recognition

Current CARs



hinge +
Transmembrane
(CD8a ... others)

CD137 / CD28 = 2nd signal - 3rd signal
(Costimulatory domain)

CD3ζ = 1st signal
(Signalling domain)



Clínic
Barcelona

UNIVERSITAT
BARCELONA

IDIBAPS
Sant Joan
de Déu

FDA / EMA CART19 / CART-BCMA approved:

Since August-October 2017 (FDA) / July 2018 (EMA) / July 2020 (FDA) / February 2022 (FDA)



Novartis ALL & DLBCL <25 y
USA: 475,000 \$ / patient)

Spain: 320 m€



NOW APPROVED



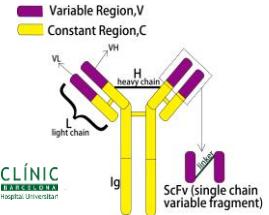
Kite NHL DLBCL:
USA 373 m\$ / patient
Spain: 320 m€

Kite MBCL Lymphoma (FDA)

CART-BCMA approved. 2022



Aim: Best treatments for our patients!!



Clone: A3-B1 (IgG2a)
1990

P. Engel, C. Serra, R.
Vilella

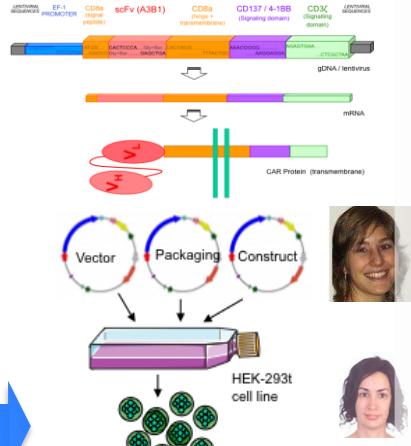


University of Pennsylvania
Manel Juan – Visiting prof.
Sabbatical by HCP-CDM

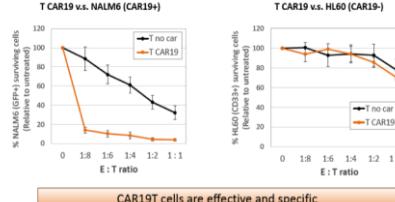


Research project
PI13/00676
PIE13/00033
PICI14/00122

CAR design & production



In vitro CAR19-mediated T cell cytotoxic activity



Preclinical steps

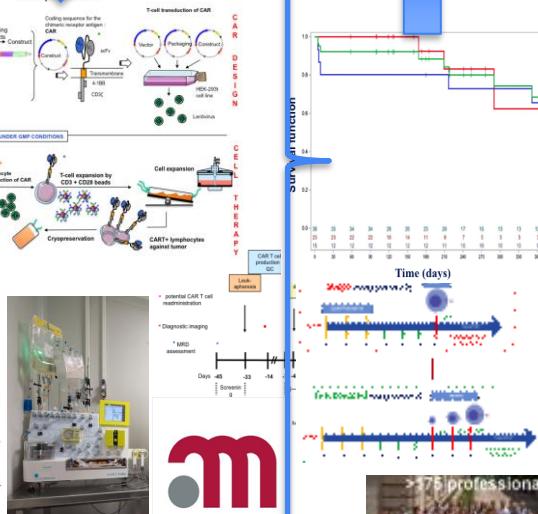
PoC proposal

ARI-0001 / CART19-BE-01
Clinical Trial

ARI Project



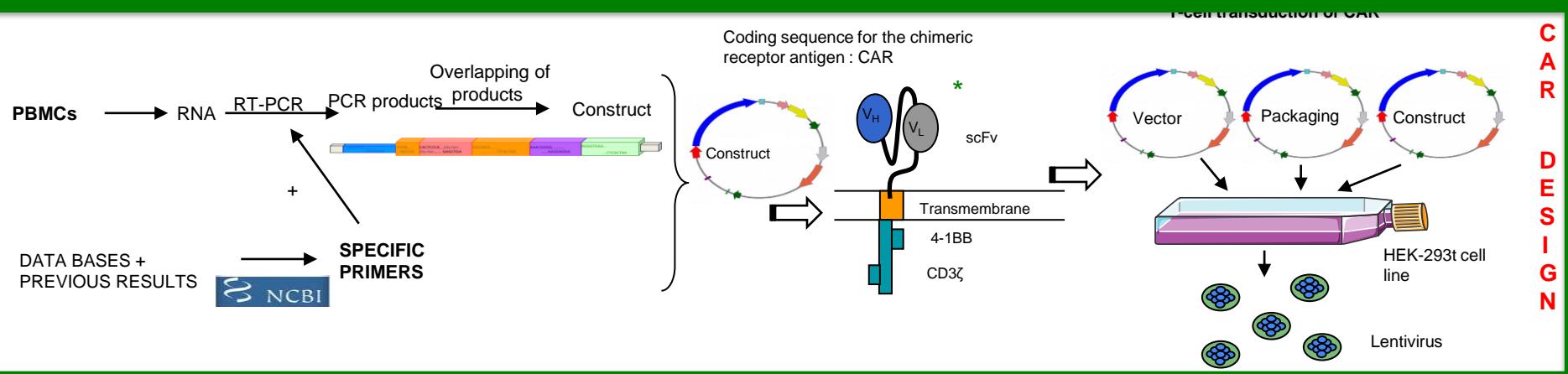
CAR production



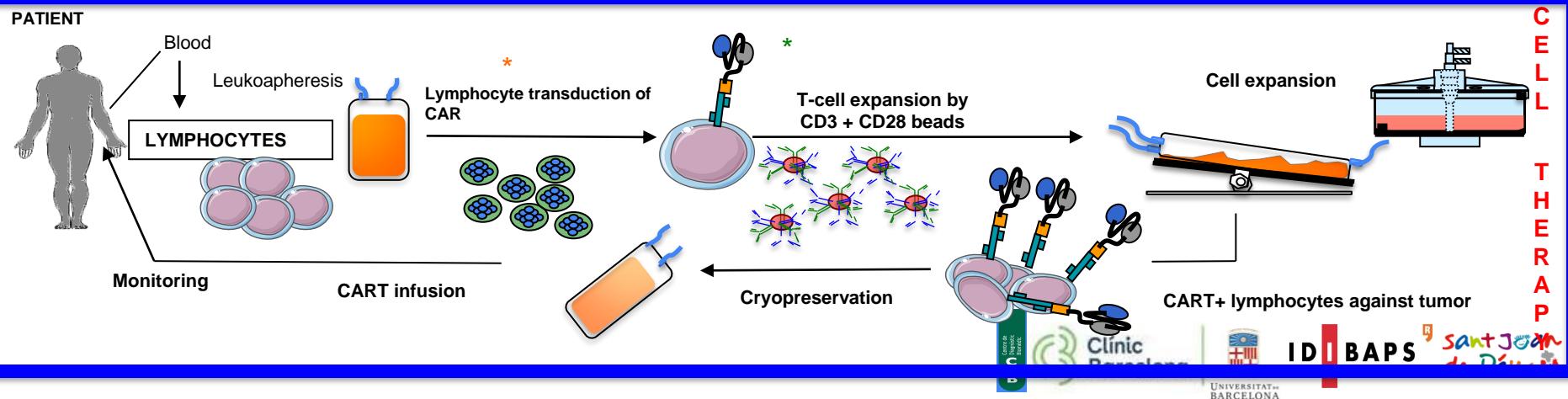
National & International Partnership

St Joan Despí

CAR production

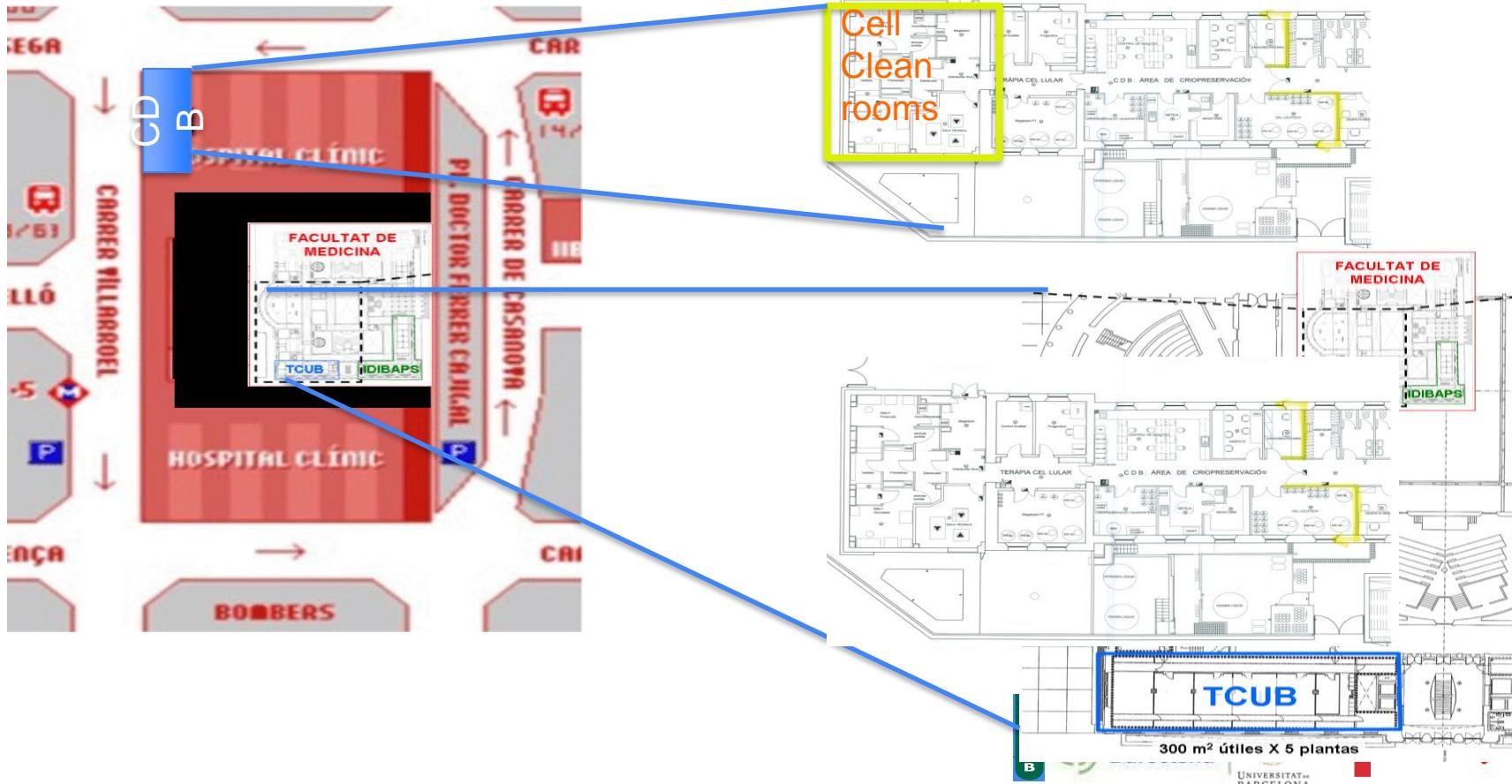


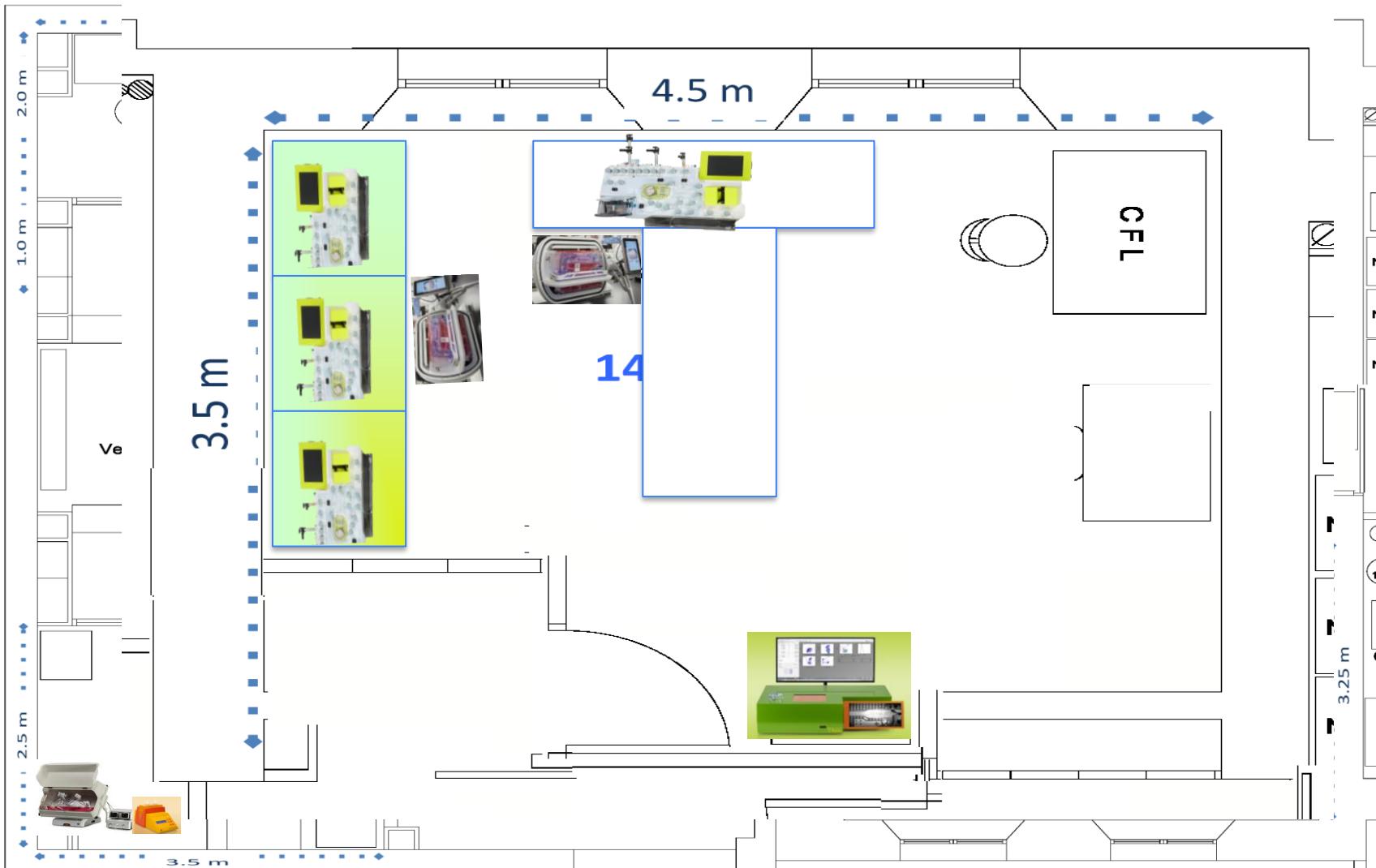
UNDER GMP CONDITIONS





GMP facilities at HCB - UB





jean
leu





Pediatric Cancer Center
(PCC)
Hospital Sant Joan de
Deu.



Leitat
C. de Pallars, 179, 185

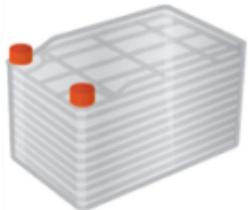


LV production system scale up: “LENTI-UP PROJECT”

Current production system



New production system



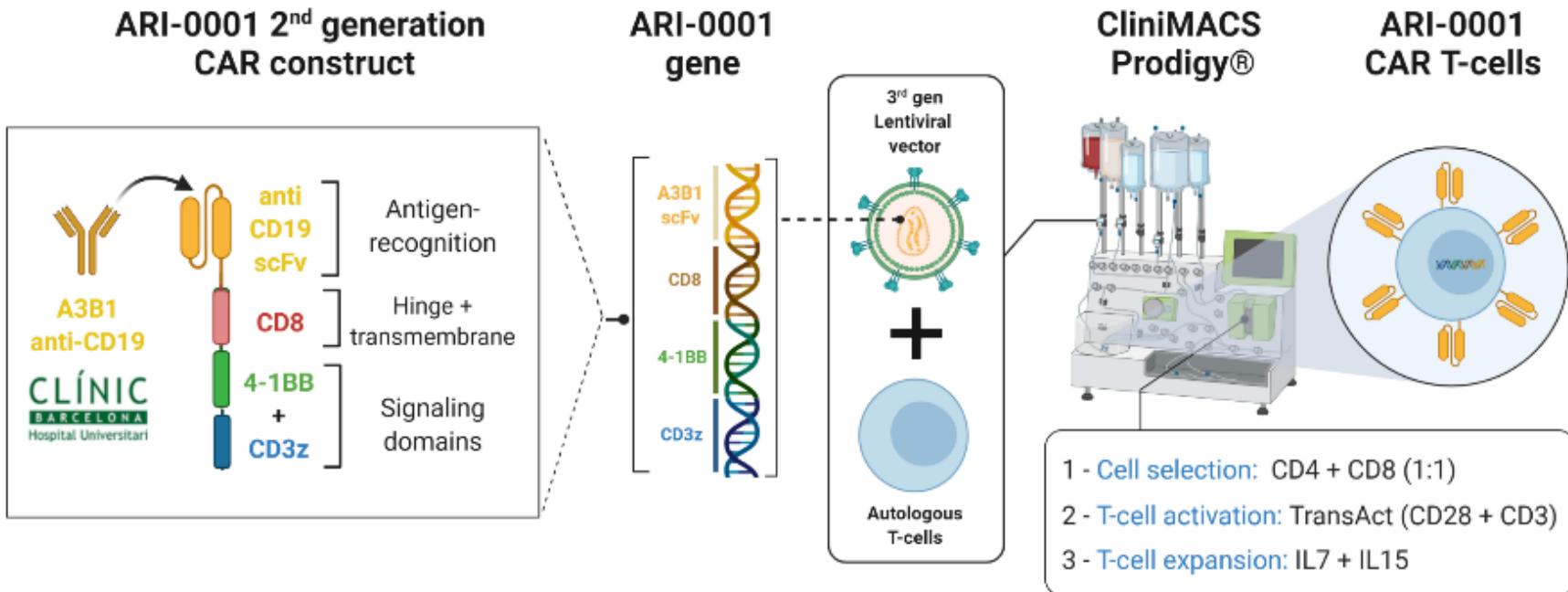
Development using Hydro:
 2.4m^2

Define conditions:

- Seeding density
- Media perfusion conditions
- Plasmid transfection conditions
(cell density, plasmid-PEI concentrations)
- Harvest conditions

“Direct” scale-up to Carbo
 10m^2 or 30m^2

ARI-0001 cells (*varnimcabtagene autoleucel* [*varnim-cel*])



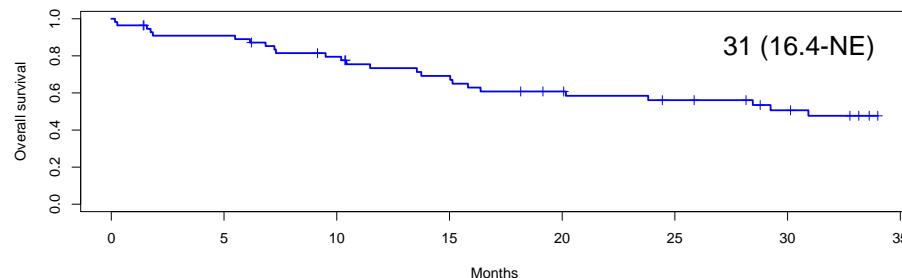
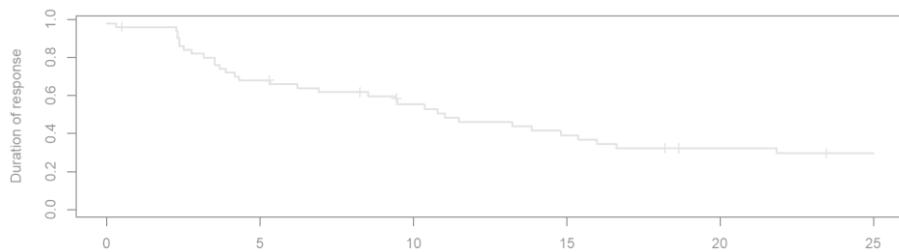
Castella M, et al. *Mol Ther*. 2019
Ortíz-Maldonado V, et al. *Mol Ther*. 2021

Eficàcia i seguretat de varnim-cel comparada amb brexu-cel en pacients adults amb leucèmia limfoblàstica aguda refractària o recaiguda

CRR

89% (79-95%)

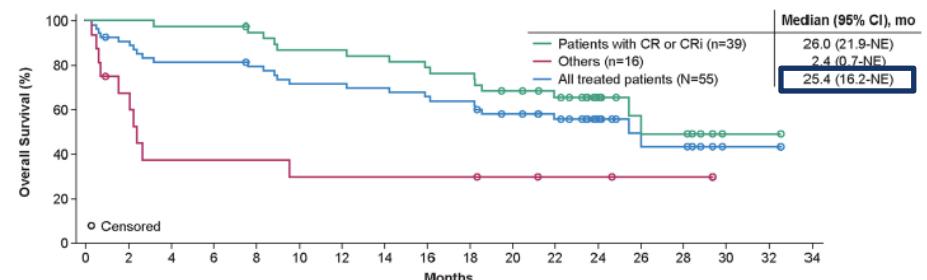
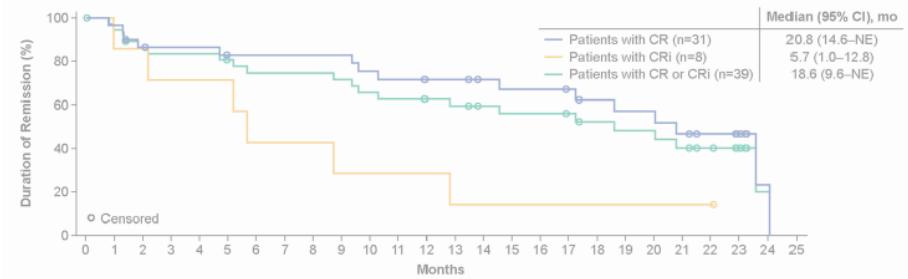
	All grades	Grade ≥ 3
CRS	52% (40-65%)	7% (3-17%)
ICANS	7% (3-17%)	0% (0-6%)



CRR

71% (57-82%)

	All grades	Grade ≥ 3
CRS	89% (78-94%)	24% (14-36%)
ICANS	60% (47-72%)	25% (16-38%)



Eficàcia i seguretat de varnim-cel comparada amb brexu-cel en pacients adults amb leucèmia limfoblàstica aguda refractària o recaiguda

CRR

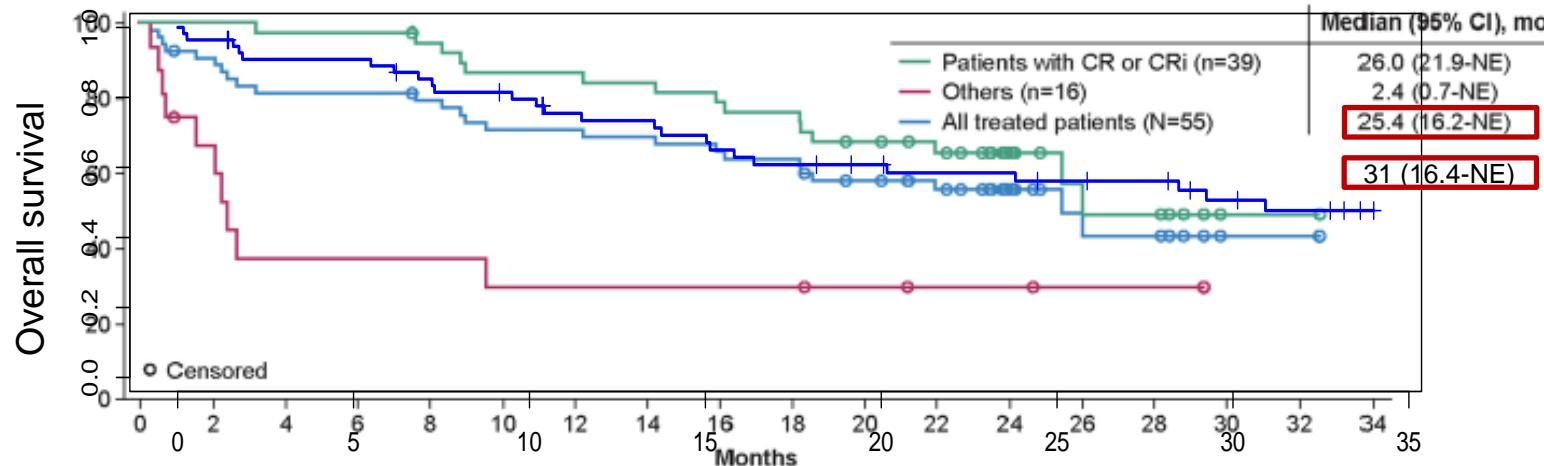
89% (79-95%)

CRR

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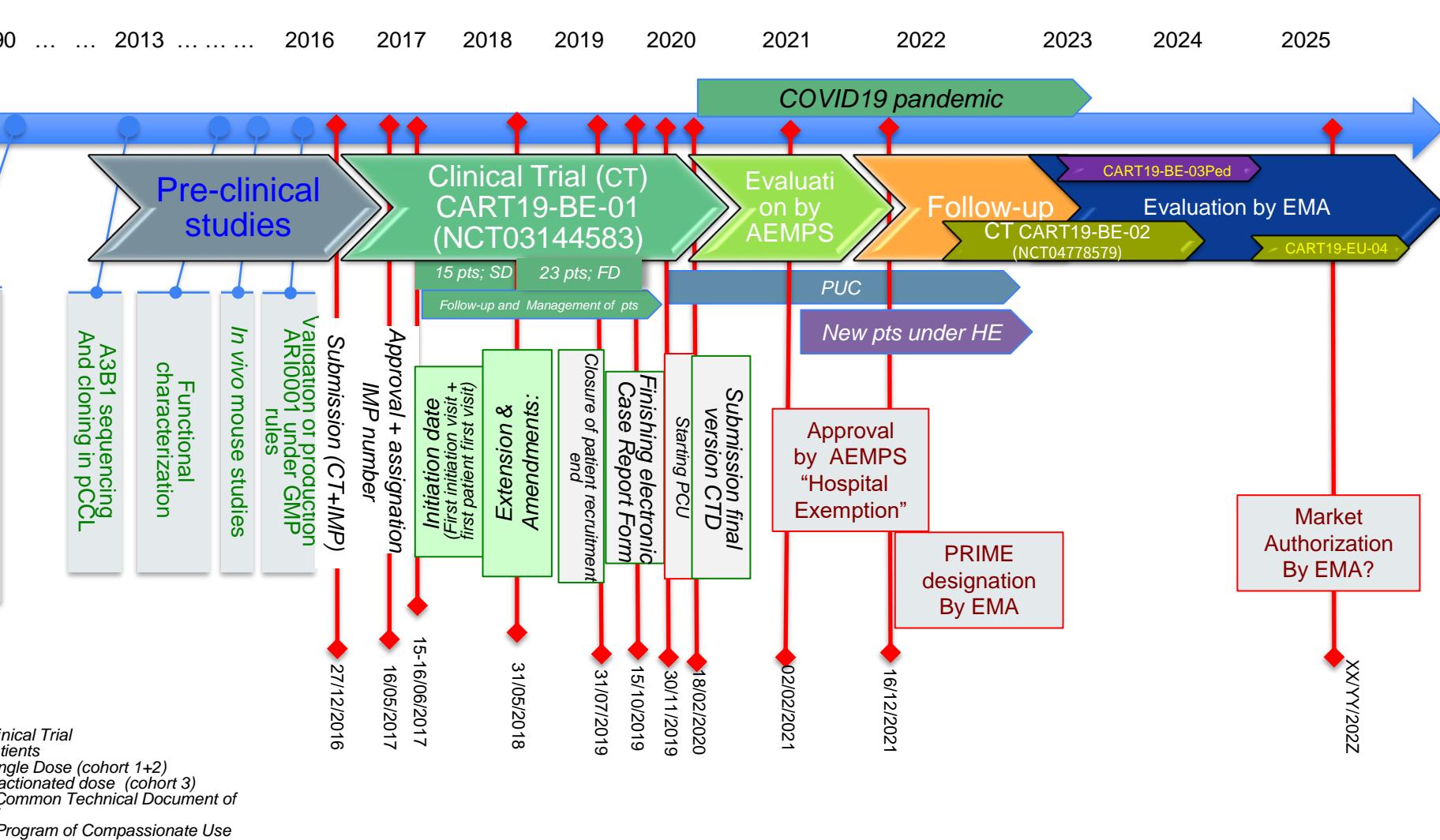
	All grades	Grade ≥ 3
CRS	89% (78-94%)	24% (14-36%)
ICANS	60% (47-72%)	25% (16-38%)



Clinic
Barcelona



IDIBAPS
Sant Joan
de Déu
Shah et al. JHO 2022



Conceder la autorización de uso del medicamento de terapia avanzada de fabricación no industrial “ARI-0001 dispersión para perfusión, que contiene $0,1\text{-}1\times10^6$ células/kg – Hospital Clínic de Barcelona ”, en el ámbito y con las condiciones que se especifican a continuación:

Código Nacional:	Formato:
730228	ARI-0001 dispersión para perfusión, que contiene $0,1\text{-}1\times10^6$ células/kg – Hospital Clínic de Barcelona, 1 bolsa de criopreservación CryoMacs de 30 ml

Agencia Española de Medicamentos y Productos Sanitarios (AEMPS)

Fecha de la firma: 01/02/2021

Puede comprobar la autenticidad del documento en la sede de la AEMPS:<https://localizador.aemps.es>

CSV: 3 T 9 K D D 8 A F 8



CORREO ELECTRÓNICO

smhaem@aemps.es

Página 1 de 5

C/ CAMPEZO, 1 - EDIFICIO 8
28022 MADRID
Tel.: 918225073
Fax: 918225043



16 December 2021
EMA/720469/2021
Human Medicines Division

Subject: Request for **eligibility to the PRIME scheme**
ARI-0001 - EMA/PRIME/21/046

With reference to your request dated 19/10/2021 for access to the PRIME scheme for ARI-0001 in the treatment of patients older than 25 years with relapsed/refractory acute lymphoblastic leukaemia (ALL), I would like to inform you that the CHMP during its December 2021 meeting has considered your justification and the recommendation from the Committee for Advanced Therapies (CAT).

Based on the claims, the justification for such claims and the description of the available data provided by the a

• Desp
olde
Access to support through the PRIME scheme is therefore **confirmed**.

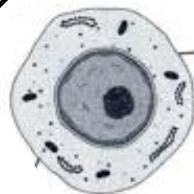
cell therapy (allo-HSCT). There is a need for improved therapies to increase remission rates, bridge patients until transplant, and ultimately improve survival in adults with relapsed/refractory ALL. Therefore, an unmet need in the proposed patient population is confirmed.

- There is a strong pharmacological rationale for use of ARI-0001 in ALL, further supported by results from a CD19+ cell-line derived xenograft mouse model showing anti-tumour activity of the product.
- Clinical data show promising efficacy of ARI-0001 in relapsed/refractory ALL patients older than 25

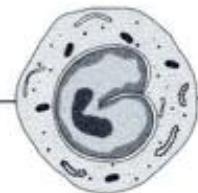
CD19

BCMA

B ALL



B Lymphoma



CD19, CD20, sIg(k/λ)



CD19, CD-20, sIg(k/λ)

Lymphoplasmocitoid



CD19, CD-20, sIg(k/λ)

CLL



CD19, CD-20
sIg(k/λ) dim, CD5

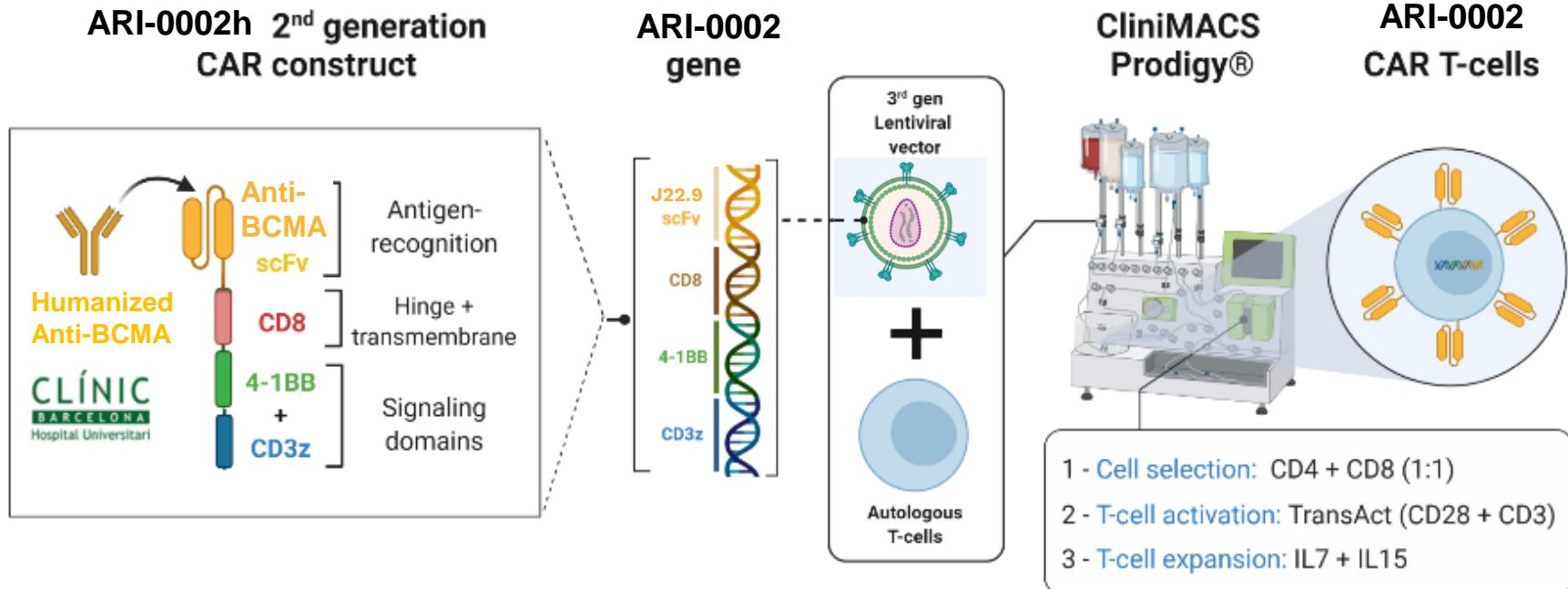
Myeloma



CD38, cIg(k/λ), CD56

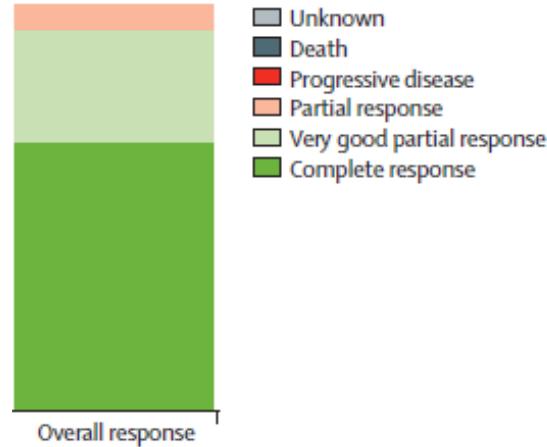
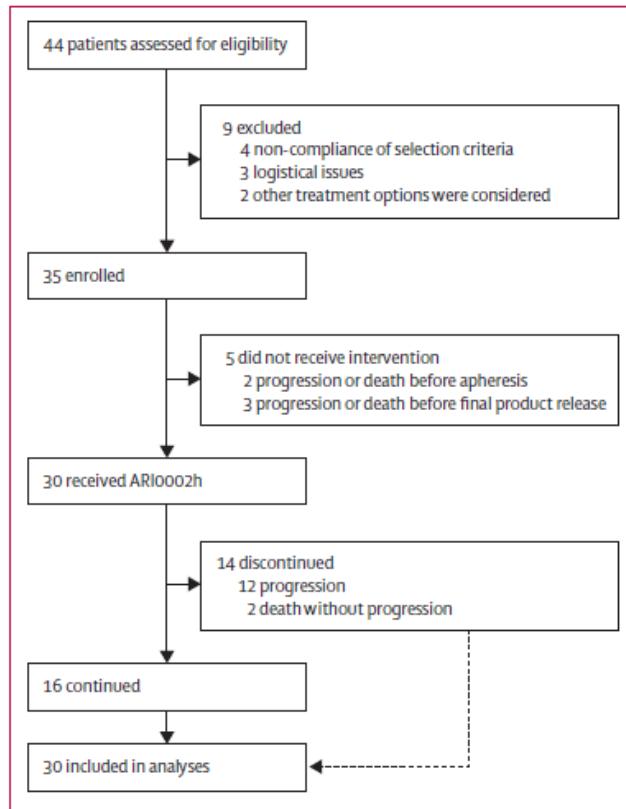


ARI-0002h cells (*cesnicaltagene autoleucel [cesni-cel]*)



Pérez-Amil L, et al. *Haematologica*. 2021

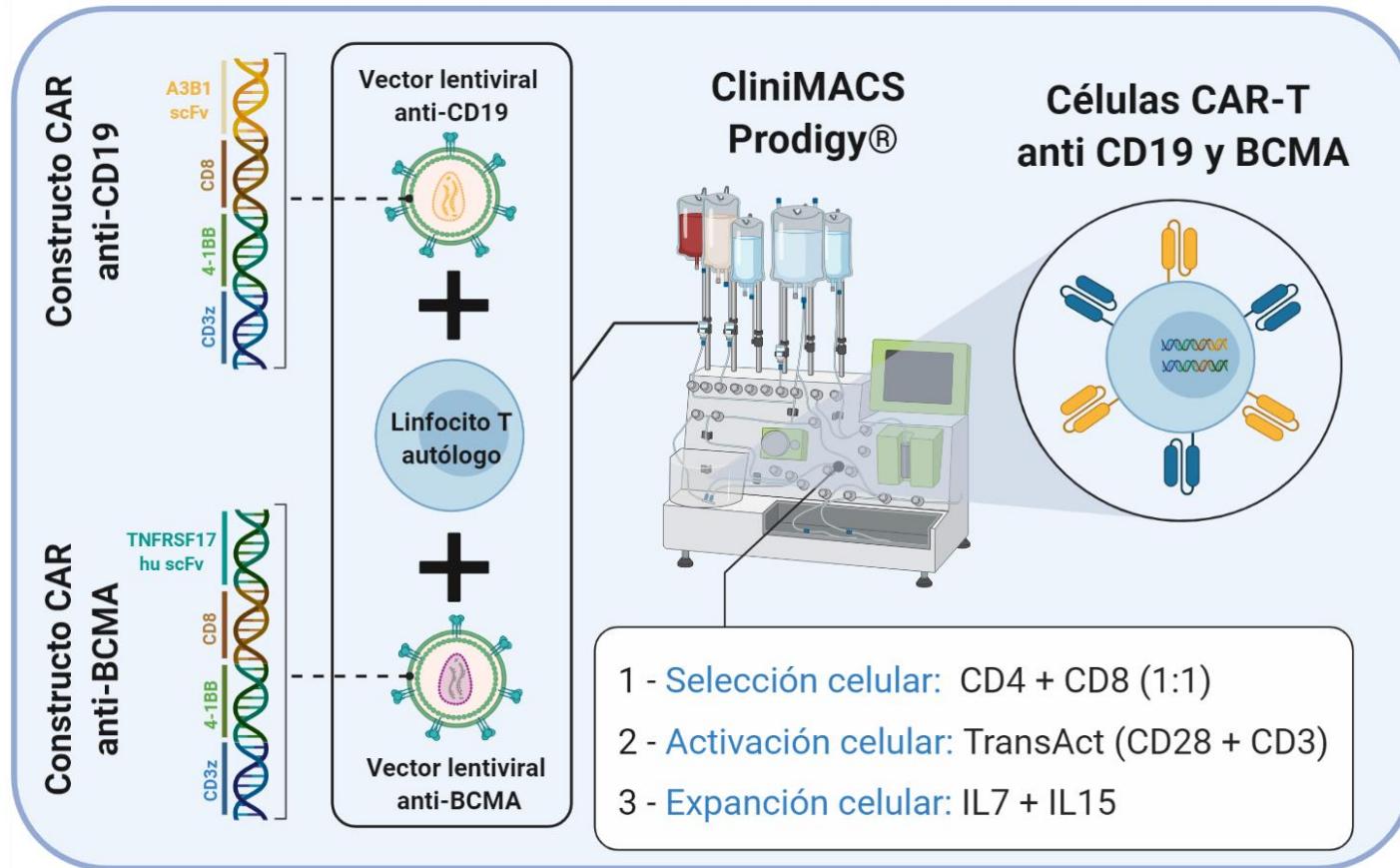
A Oliver-Caldès, et al. *Lancet Oncology* 2023

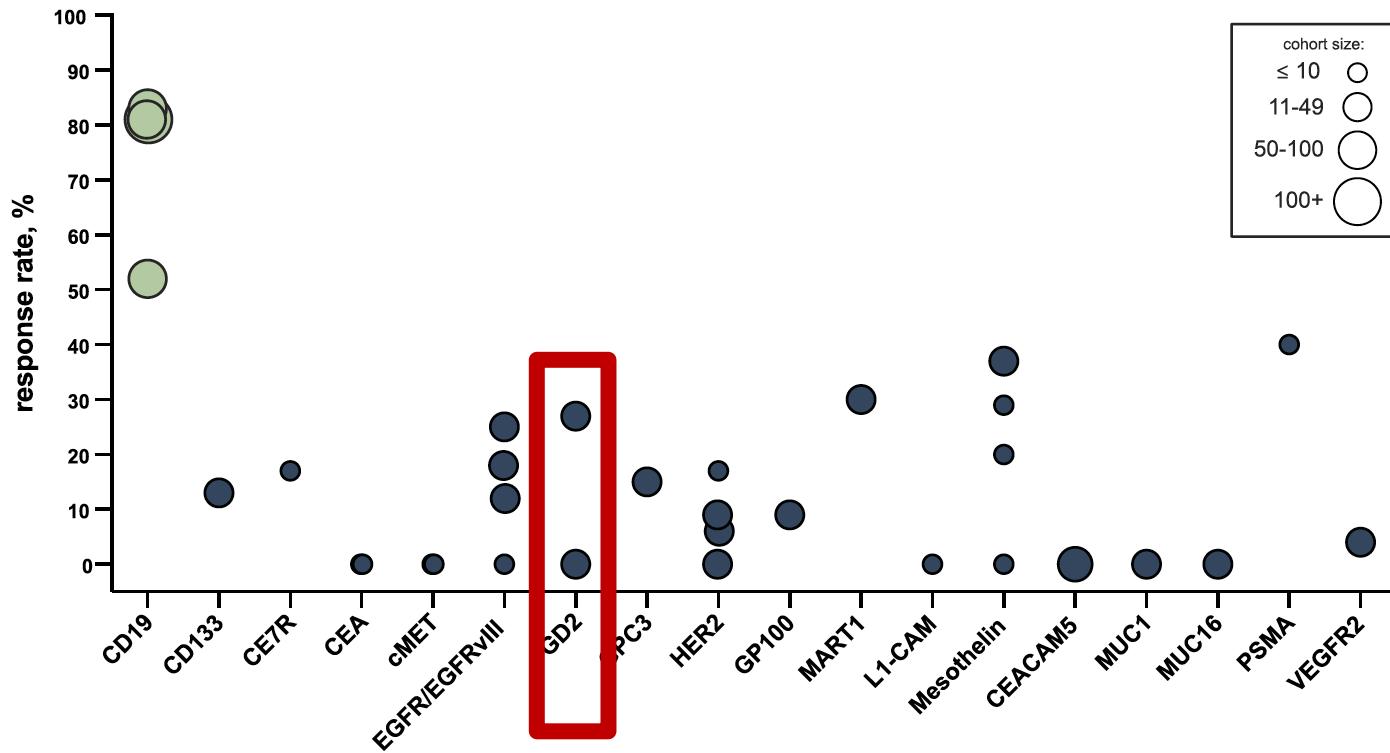


	Grade 1	Grade 2	Grade 3-4
Cytokine release syndrome	15/24 (63%)	9/24 (38%)	0
Immune effector cell-associated neurotoxicity syndrome	0	0	0
Infusion reaction	1/30 (3%)	0	0
Tumour lysis syndrome	0	1/30 (3%)	0
Persistent cytopenias	0	0	20/30 (67%)

Oliver-Caldés et al. Lancet Oncol 2023

What is ARI-0003?





Schoenfeld and O'Cearbháill .The Cancer Journal. 27(2):134-142, 2021



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ANTITUMORAL TARGETS (and others) with CAR-T (in HCB/HSJD)

Hematological tumors:

- **CD19** – B-Leukemia & Lymphomas

Kymriah® o *tisagenlecleucel*,
Yescarta® o *axicabtagene ciloleucel*,
Tecartus® o *brexucabtagene autoleucel*
Breyanzi® o *lisocabtagen maraleucel*

ARI-0001 o *varnimcabtagene autoleucel*

- **CD269 /BCMA** – Multiple myeloma

Abecma® o *idecabtagene vicleucel*
Carvykti o *ciltacabtagene autoleucel*

ARI-0002h

- **CD7, CD1a** – T lineage
- **CD123, Gya-1, ... , - LMA**

Solid tumors

- **HER2 (4D5 variant)**– BC, OC.,
...
• **IL13Ra** – GBM
- EGFR-viii
- Mesothelin
- **PSMA** – C.P.
-

Autoimmunity, Tx rejection, ...

- DSG - Penfigo, ...
- **CAAR-HLA_A*2** – rejection, ..
- CAR-Treg
-



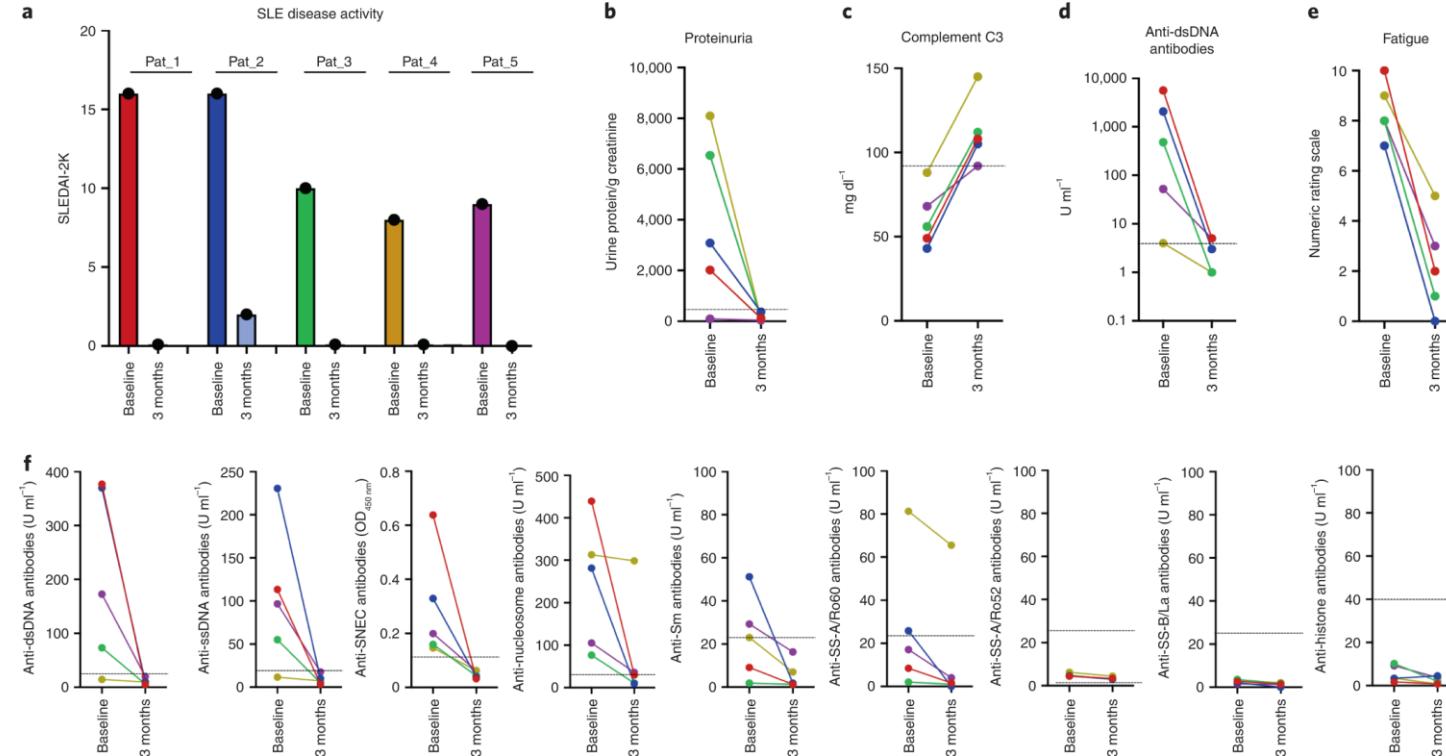
World Exclusive: CAR-T Cell Therapy Successfully Used Against Autoimmune Disease (Medicine)

[13 AUG 2021](#) | JAISRIPADHI | LEAVE A COMMENT

Anti-CD19 CAR T cell therapy for refractory systemic lupus erythematosus

Andreas Mackensen^{1b,2,8}, Fabian Müller^{1,2,8}, Dimitrios Mougiaikakos^{1,2,3,8}, Sebastian Böltz^{1b,2,4}, Artur Wilhelm^{1b,2,4}, Michael Aigner^{1,2}, Simon Völkl^{1,2}, David Simon^{1b,2,4}, Arnd Kleyer^{1b,2,4}, Luis Munoz^{2,4}, Sascha Kretschmann^{1,2}, Soraya Kharboutli^{1,2}, Regina Gary^{1,2}, Hannah Reimann^{1b,2}, Wolf Rösler^{1,2}, Stefan Uderhardt^{2,4}, Holger Bang⁵, Martin Herrmann^{1b,2,4}, Arif Bülent Ekici^{1b,6}, Christian Buettner⁶, Katharina Maria Habenicht⁷, Thomas H. Winkler^{1b,7}, Gerhard Krönke^{1b,2,4,8} and Georg Schett^{1b,2,4,8✉}

5 pacientes con LES (4 mujeres +1 hombre) de 22 (6) años, duración 4 (8) años y enfermedad activa: 16 (8) refractarios a varios tratamientos farmacológicos inmunosupresores reciben CART19.



KNOWLEDGE

Academy

?

HYPOTHESIS

RESULTS

THESIS

SOLUTION



Drug

IMP



Academy

Clinical Trials

Mont Jean-Dore

Conclusions

Academic CART-cell development is possible

Requires a change of mentality

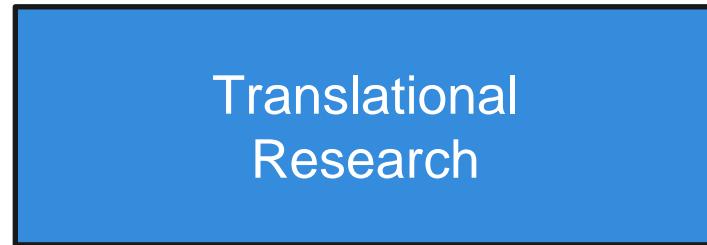
Requires help from experts in regulation

Requires stamina → Big Pharma isn't entirely happy with the current situation (e.g. they **dislike** the Hospital Exemption Clause)

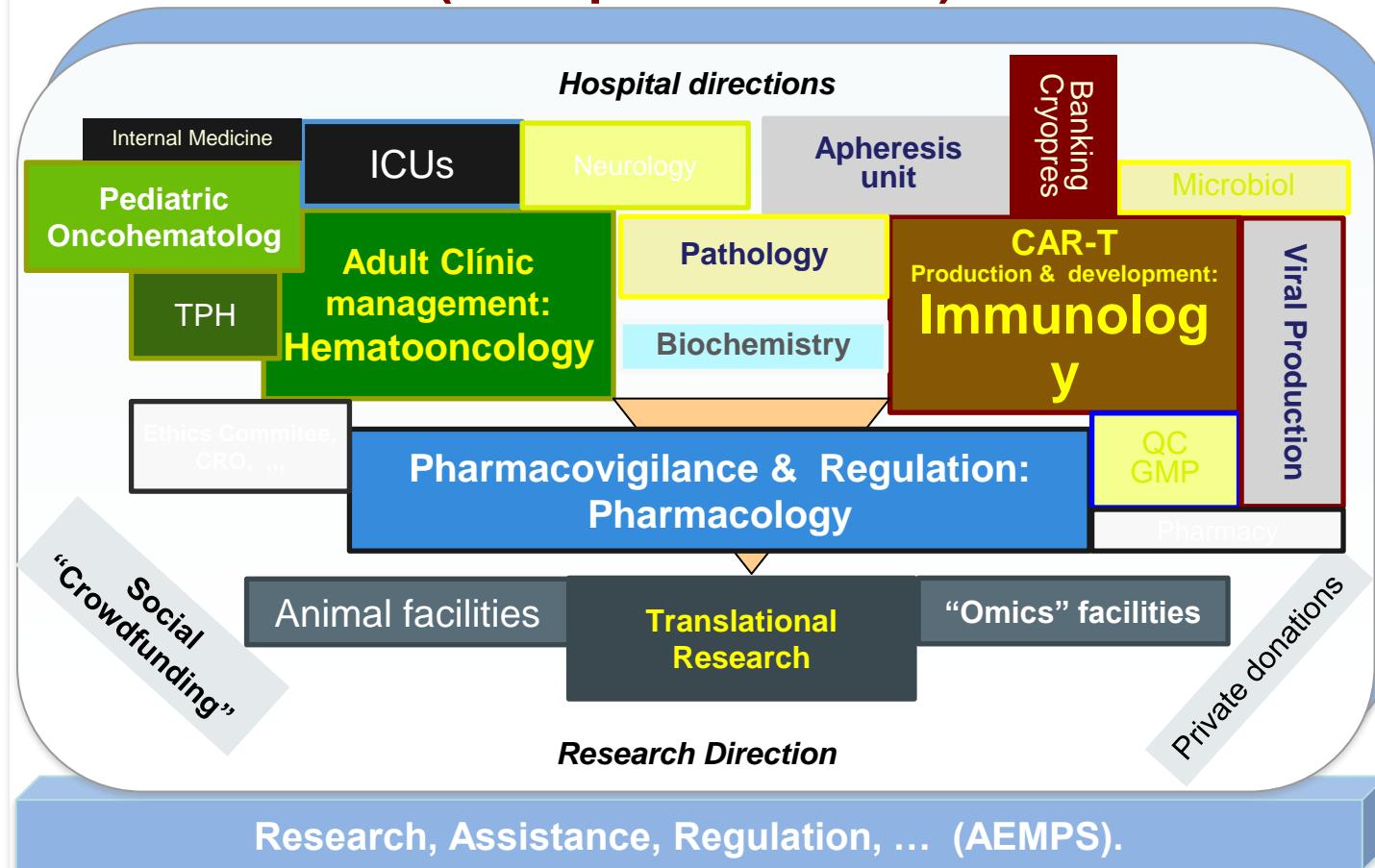
“Where there is a will, there is a way”, ... if we are flexible.

Slide adapted of the initial proposal of Dr. Delgado





How is involved in our “ARI program”? (**>200 professionals**)



Qui està involucrate en el nostre “Programa ARI”? (>280 professionals)





SANT JOAN DE DÉU



ARI ASSISTÈNCIA
RECERCA
INTENSIVA

Per la LEUCÈMIA I TRASPLANTAMENTS
HOSPITAL CLÍNIC



Institut de Recerca
CONTRA LA LEUCÈMIA
Josep Carreras



Generalitat
de Catalunya



Fundación Bancaria
"la Caixa"



CatSalut



Fundació Glòria Soler



Servei Català
de la Salut



Instituto de Salud Carlos III



Generalitat de Catalunya
Departament de Recerca
i Universitats



BARCELONA

Financiado por la Unión Europea
NextGenerationEU

Immunology

Mariona Pascal

Marta Español

E. Azucena González-Navarro

Daniel Benítez, Raquel Cabezón

Natalia Egri, Carlota García-Hoz, María Sánchez,

Jordi Yagüe

Miguel Caballero, Anna Boronat,

Maria Castellà, Hugo Calderón,

IDIBAPS

Guillermo Suñé

Beatriz Martín Antonio

Lorena Pérez-Amill

Sonia Guedan

Nela Klein,

Elias Campo, ...

IJC

Pablo Menéndez

Clara Bueno

Julio Castaño (BST), ...



AT Unit - GeneVector

Esteve Trias, ...

CTU

Sara Varea, Eulàlia Olesti, Joan Albert Arnaiz, ...

Creatio UB

Josep Maria Canals

Pere Martínez

.piñá, ...

Hospital management

Josep M. Campistol

Antoni Castells

Aurea Mira

Manel del Castillo

Miquel Pons

Adult Hematology

Julio Delgado

Valentín Ortiz

Carlos Fdez Larrea

Eva Giné

Gerardo Rodríguez

Aina Oliver, Àlex Bataller

Armando López-Guillermo

Jordi Esteve

Álvaro Urbano-Ispizua, ...

AEMPS

Collaborators:

Upenn, UCLA,

BST, 12-O, CUN, HUS,

HAM, HUVR, SERGAS-

CHUS, HRyC, Ozkaidetza,

Pediatric Hematology (HSJD)

Susana Rives

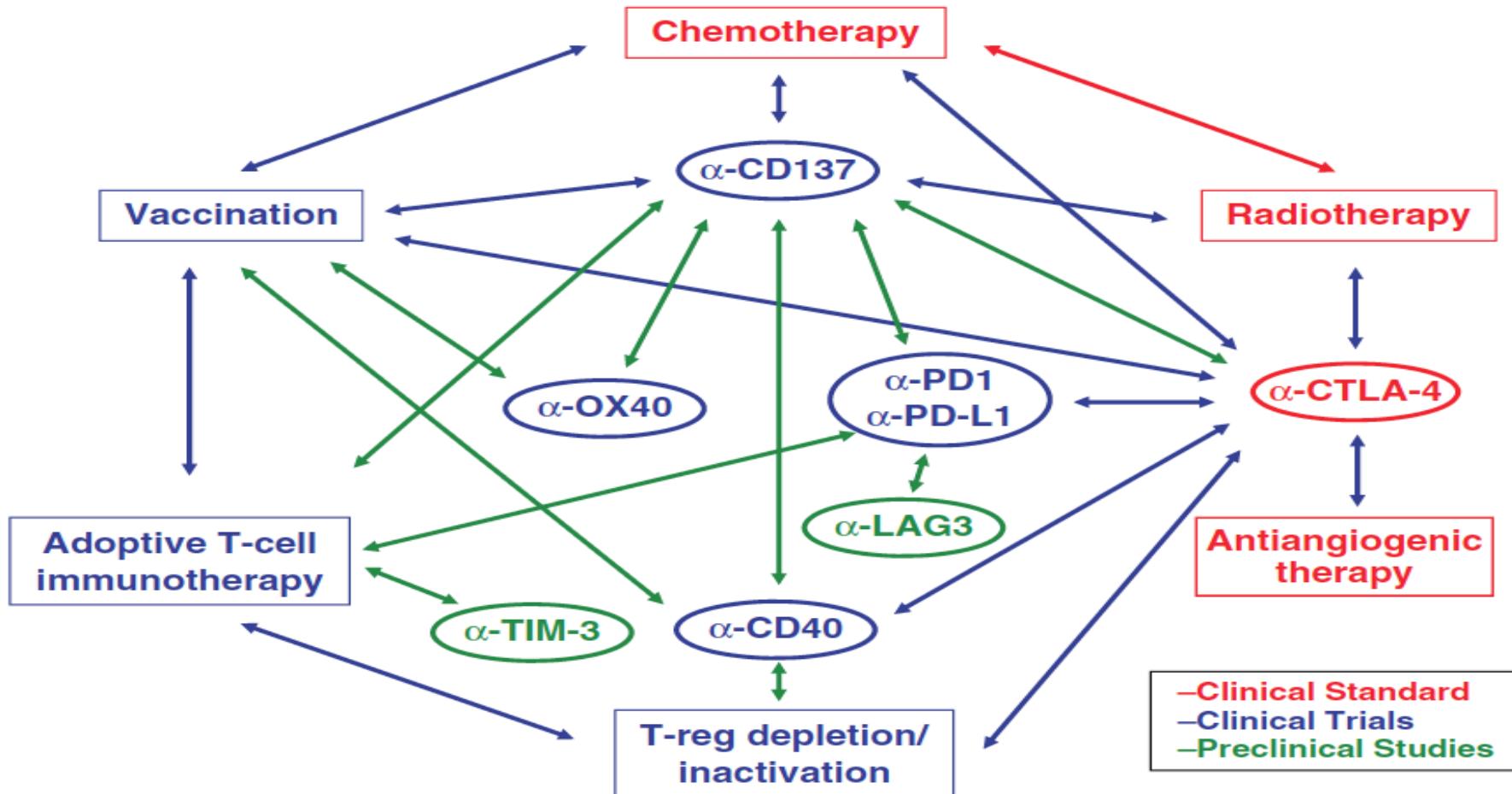
Anna Alonso

Montse Torrabadell,

Oncology

Aleix Prat

Núria Chic, ...





Moltes Gràcies!

Grazie mille!!!

Danke schön!

Obrigado!

Thanks !

謝謝你！

ありがとう！

ধন্যবাদ!

Дякую тобі!

shukra!

Merci !



Questions?

mijuan@clinic.cat