Pr Steven Le Gouill, MD, PhD

15 juin 2023

CAR-T cells in real life: the French experience, DESCAR-T registry

ENSEMBLE, PRENONS
LE CANCER DE VITESSE

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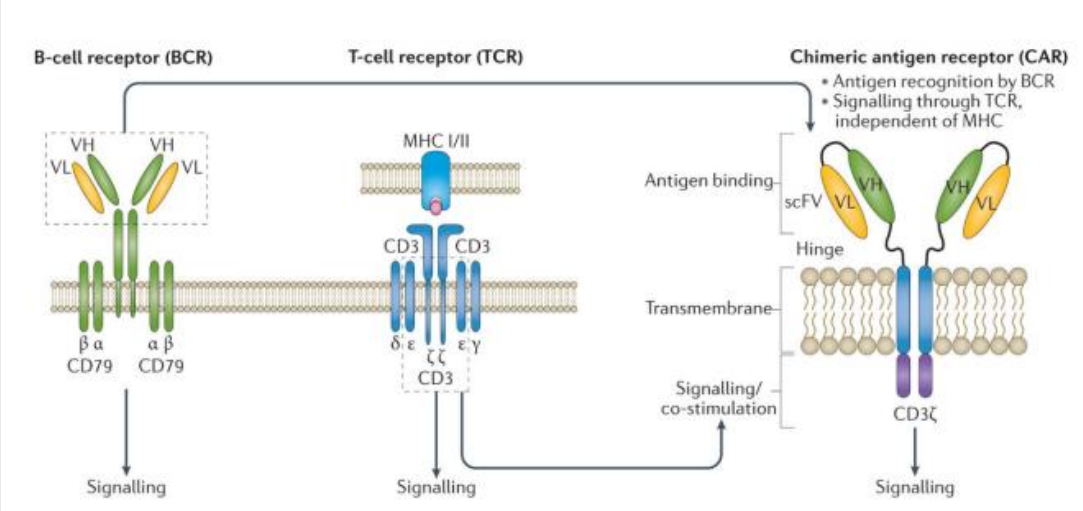
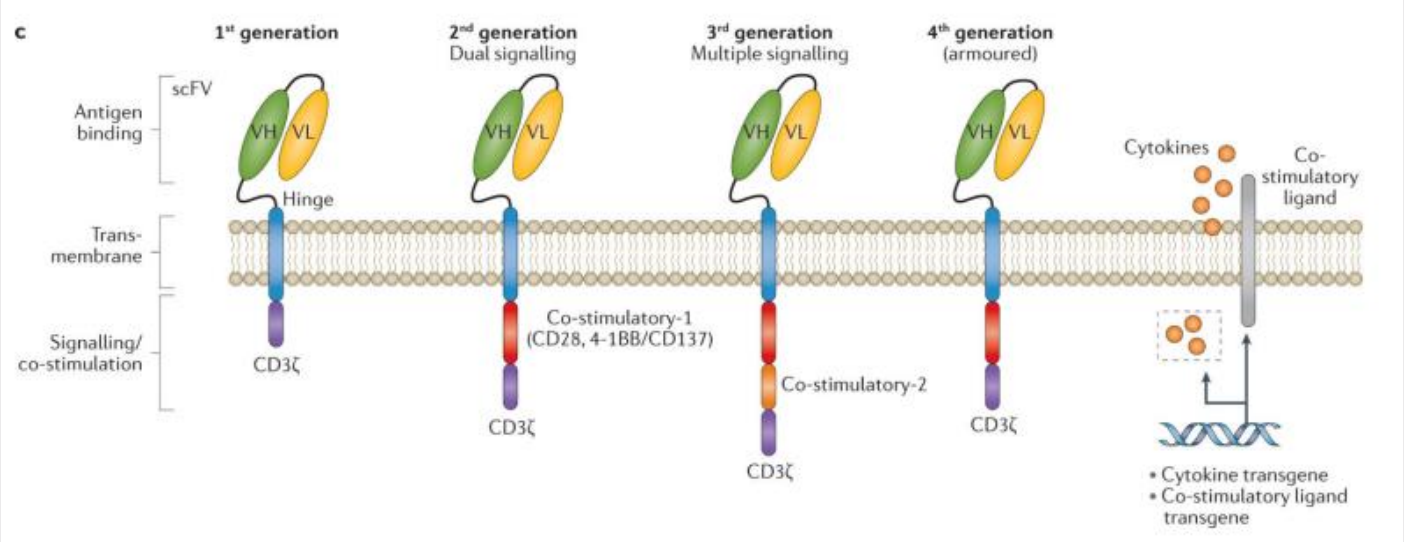
CAR-T cells





Batlevi et al, Nat Rev Clin Oncol. 2016

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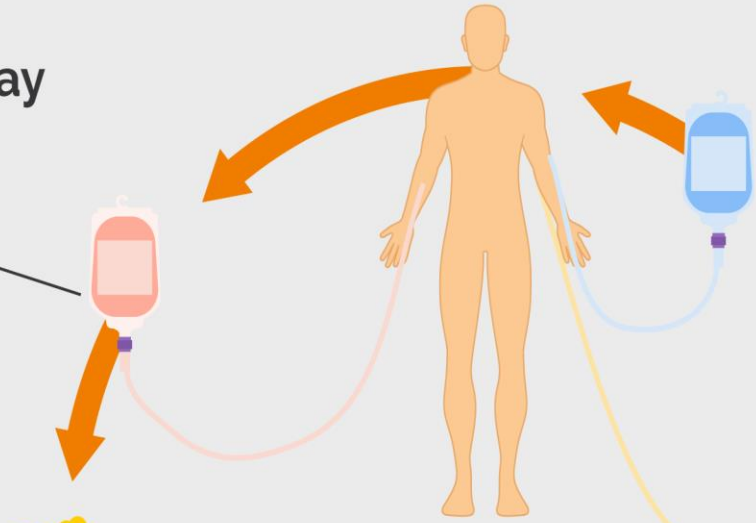
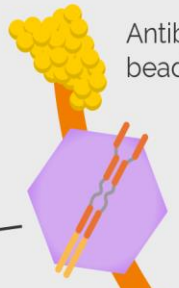
Autologous CAR-T Manufacturing delay

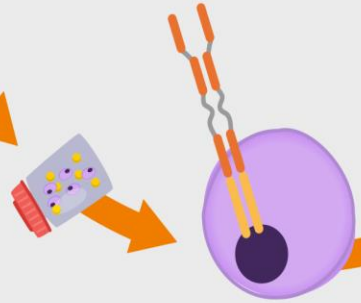


1. Leukapheresis

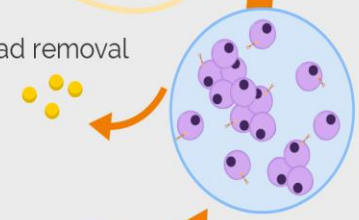


Antibody-coated beads

2. T-cell activation/ transduction*



3. Modified T-cell expansion*



Bead removal

4. Chemotherapy

5. Modified T-cell infusion

*Cellular reprogramming and ex vivo expansion are conducted at a cell processing facility.

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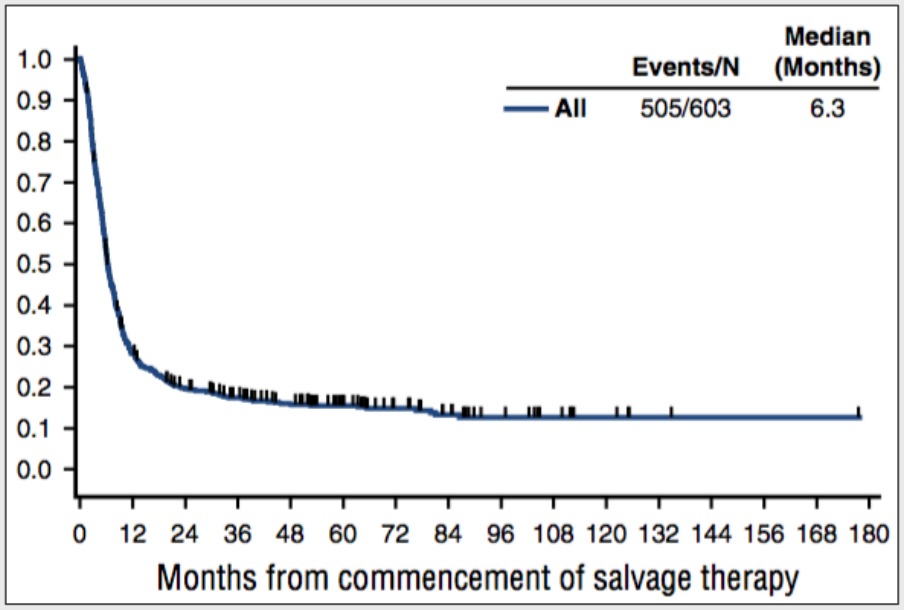


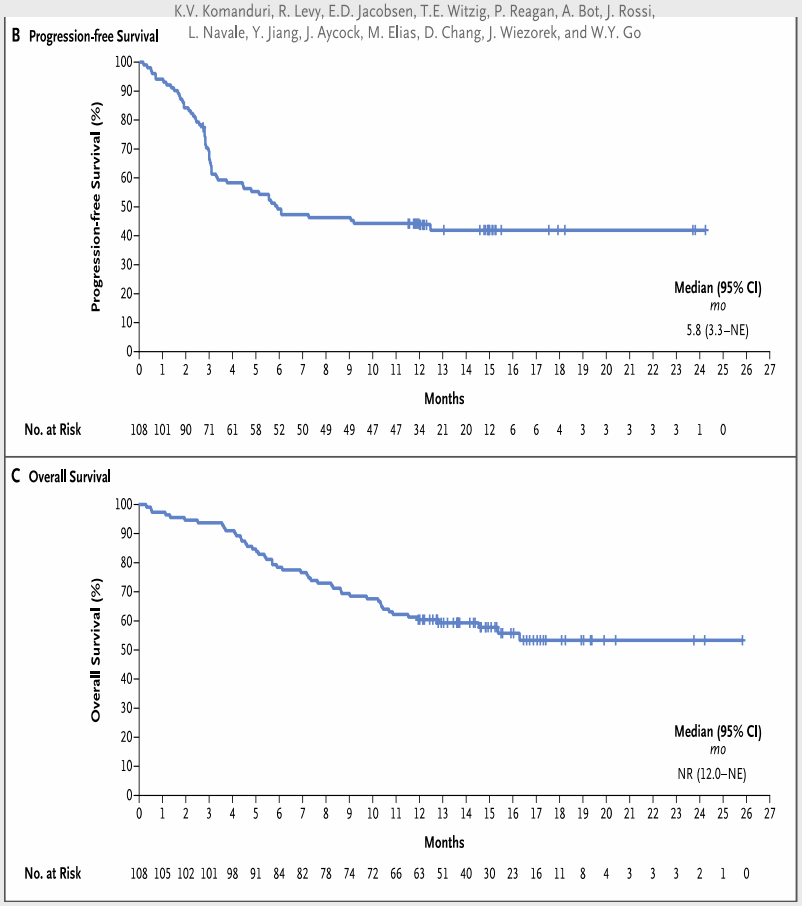
Crump et al, Blood 2017

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Axicabtagene Ciloleucel CAR T-Cell Therapy in Refractory Large B-Cell Lymphoma

S.S. Neelapu, F.L. Locke, N.L. Bartlett, L.J. Lekakis, D.B. Miklos, C.A. Jacobson, I. Braunschweig, O.O. Oluwole, T. Siddiqi, Y. Lin, J.M. Timmerman, P.J. Stiff, J.W. Friedberg, I.W. Flinn, A. Goy, B.T. Hill, M.R. Smith, A. Deol, U. Farooq, P. McSweeney, J. Munoz, I. Avivi, J.E. Castro, J.R. Westin, J.C. Chavez, A. Ghobadi, K.V. Komanduri, R. Levy, E.D. Jacobsen, T.E. Witzig, P. Reagan, A. Bot, J. Rossi, L. Navale, Y. Jiang, J. Aycock, M. Elias, D. Chang, J. Wiezorek, and W.Y. Go



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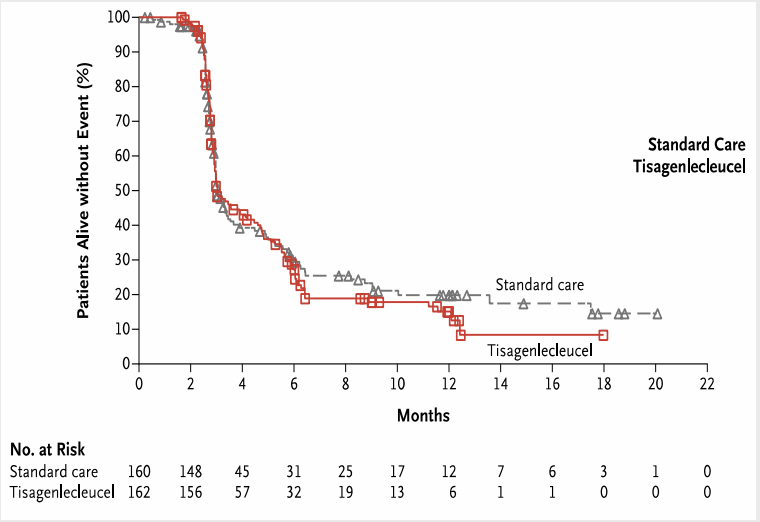
CAR-T cells in 3rd line DLBCL

CAR-T cells		Axi-Cel (Yescarta®)	Tisa-Cel (Kymriah®)	Liso-Cel (JCAR017)
References	Reference	Locke FL et al. Lancet Oncol. 2019 Jacobson C et al, ASH 2020 (#1187)	Schuster SJ et al. NEJM 2019 Jeager U et al, ASH 2020 (#1194)	Abramson JS et al. Lancet 2020
	Company	Kite-Gilead	Novartis	Juno/Celgene
	Study name	ZUMA-1	JULIET	TRANSCEND NHL 001
Patients	Median age (min-max)	58 (23-76)	56 (22-76)	63 (18-86)
	N treated patients	**108** (91%)	**111** (67%)	**269** (78%)
	Lymphoma subtype	DLBCL / PMBCL / TFL	DLBCL / TFL	DLBCL / TiNHL / PMBL / FL3B
Efficacy	Median follow-up	51.1 months	40.3 months	18.8 months
	Best ORR	**83%**	**52%**	**73%**
	Best CR	**58%**	**40%**	**53%**
	Median PFS	5.9 months	2.9 months	6.8 months
	Median OS	**25.8 months**	**12 months**	**21.1 months**
Toxicity	Grade ≥ 3 CRS	11%	23%	2%
	Grade ≥ 3 ICANS	32%	11%	10%

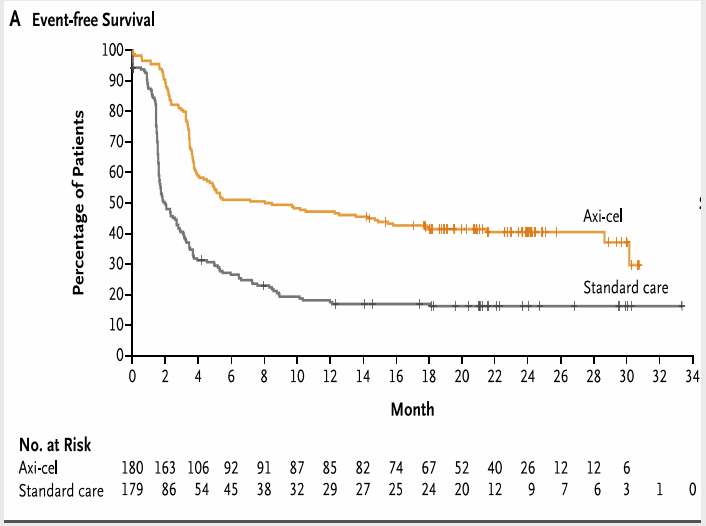
CAR-T at first relapse vs SOC

				CAR-T vs SOC		
CAR-T	**Ref**	**Design**	**N**	**mEFS (months)**	**mOS**	**Superiority CAR-t vs SOC**
Tisagenlecleucel (Belinda trial)	Bishop et al. Nejm 2022	phase III	322	3 vs 3 (P=0.61)	immature at data cutoff	No
Axicabtagene Ciloleucel (Zuma 7)	Locke et al. Nejm 2022	phase III	359	8.3 vs 2 (P<0.001)	NR vs 35.1m (P=0.054)	Yes for EFS but not OS
Lisocabtagene maraleucel (Transform)	Kamdar et al. Lancet , 2022	phase III	232	10·1 vs 2.3 (p<0·0001)	NR vs 16.4m (p=0·026)	Yes for EFS and OS

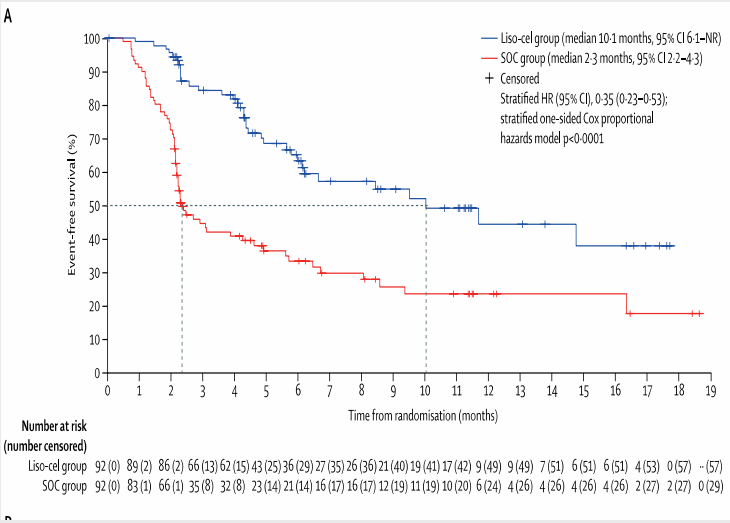
Tisagenlecleucel (Belinda)



Axicabtagene Ciloleucel (Zuma 7)



Lisocabtagene maraleucel (Transform)



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DESCAR-T

Dispositif d'Etude et de Suivi des CAR-T
French CAR-T registry

DESCAR-T Registry

Journées du LYSA
Lille, 14 October 2022

Roch Houot, MD, PhD
Professor of Hematology
Rennes University Hospital
Rennes, France

Steven Le Gouill, MD, PhD
Professor of Hematology
Director of Institute Curie Comprehensive Cancer Center
Paris, France

DESCAR-T : 3 objectives

Scientific

Improve our knowledge and understanding of the mechanisms associated with CAR T-cells efficacy and toxicity in real life

Regulatory

Address request from the French Health Authorities (HAS) : provide real life data of patients treated with CAR T-cells

Administrative

CAR T-cell reimbursement

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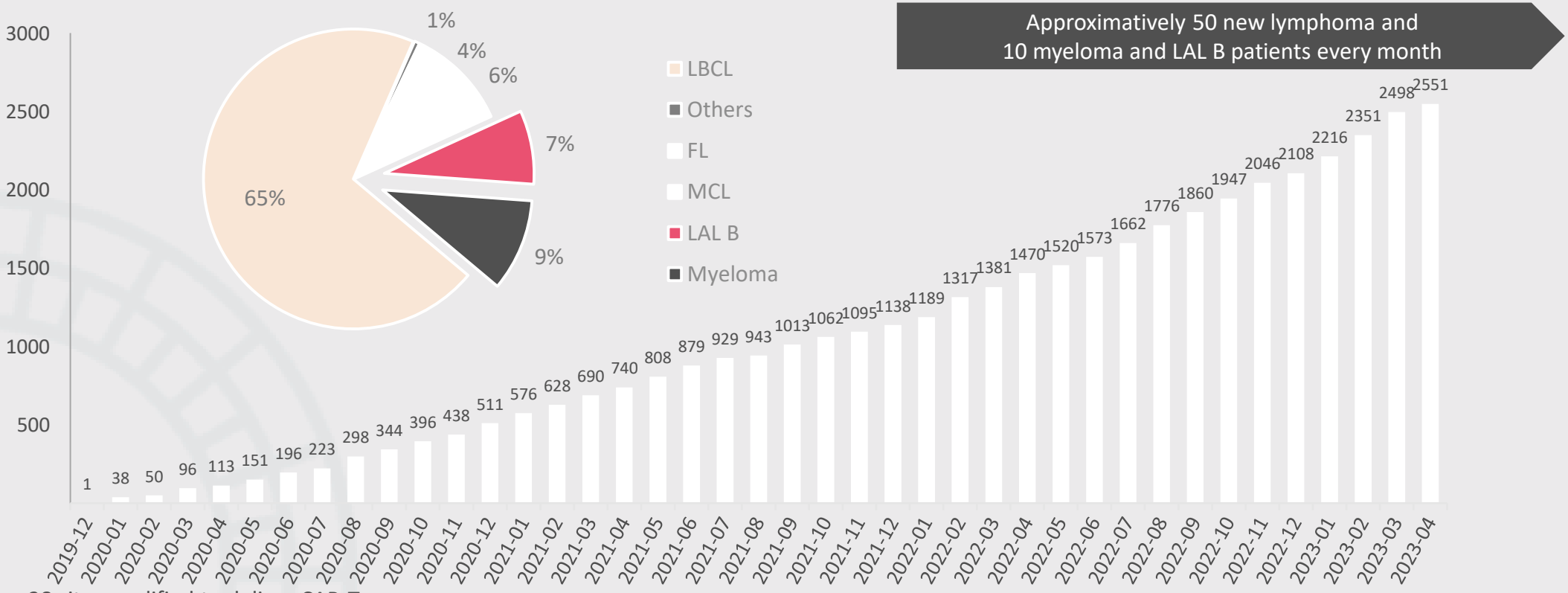
DESCAR-T Registry: Cumulated Recruitment

April 2023
2500 patients in the registry!

Approximatively 50 new lymphoma and
10 myeloma and LAL B patients every month



- 38 sites qualified to deliver CAR-T

FIRST RESULTS OF DLBCL PATIENTS TREATED WITH CAR-T CELLS AND ENROLLED IN DESCAR-T REGISTRY, THE FRENCH REAL-LIFE DATABASE FOR CAR-T CELLS IN HEMATOLOGIC MALIGNANCIES

Steven Le Gouill[1], Emmanuel Bachy[2], Roberta Di Blasi [3], Guillaume Cartron[4], Favid Beauvais[5], Fabien Le Bras[6], François-Xavier Gros [7], Sylvain Choquet [8], Pierre Bories[9], Marie-Thérèse Rubio[10], René-Olivier Casasnovas[11], Jacques-Olivier Bay[12], Mohamad Mohty[13], Jean-Pierre Marolleau[14], Thomas Gastinne[1], Pierre Sesques[2], Jean-Jacques Tudesq[4], Franck Morschhauser[5], Elodie Gat[15], Florence Broussais[15], Catherine Thieblemont[3], Roch Houot[16]

Affiliations: *[1]CHU Nantes, Nantes, [2]HCL, Lyon, [3]APHP-Hopital Saint-Louis, Paris, [4]CHU Montpellier, Montpellier, [5]CHU Lille, Lille, [6]APHP-Créteil, Créteil, [7]Hematology and cell therapy department, Bordeaux, [8]APHP- La Pitié , Paris, [9]IUCT Oncopole, Toulouse, [10]CHU Nancy, Nancy, [11]CHU Dijon, Dijon, [12]Service de thérapie cellulaire et d'hématologie clinique adulte, CHU Clermont-Ferrand, site Estaing, Clermont-Ferrand, [13]AP-HP Saint Antoine, Paris, [14]CHU Amiens, Amiens, [15] LYSARC, Lyon, [16]CHU Rennes, Rennes, France*

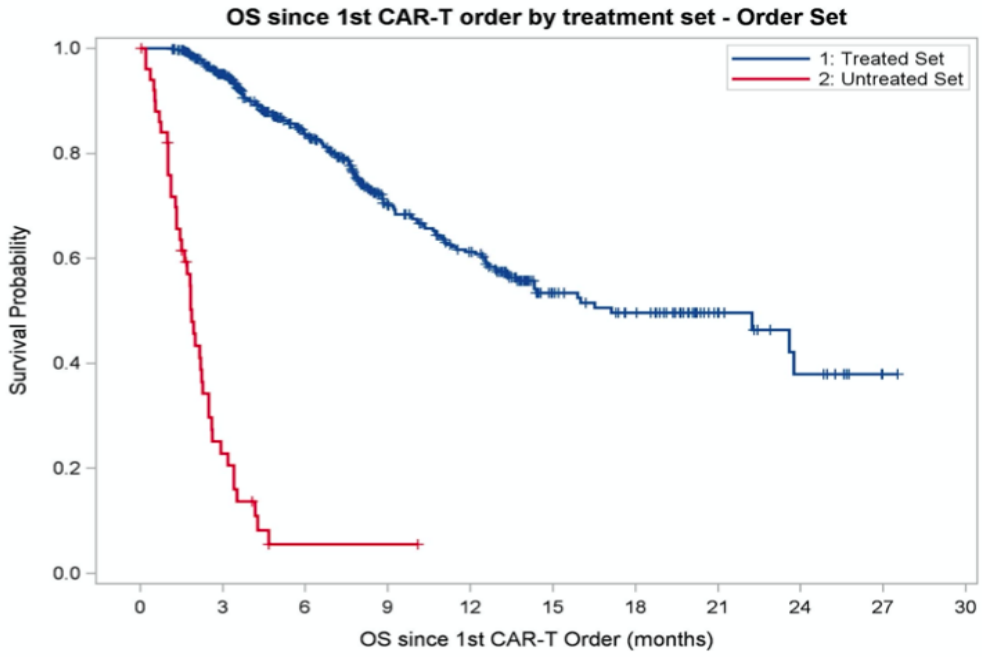
Program section: Aggressive lymphoma - CAR-T & transplant
Abstract S216

DESCAR-T: main results

	Toxicities within 10d post CAR-T (data available in 515 pts)
CRS (all grades)	418 (81.2%)
grade 1-2	373
grade ≥ 3	44
missing	1
Neurotoxicity (all grades)	184 (35.7%)
grade 1-2	133
grade ≥ 3	50
missing	1
grade ≥ 3 opportunistic or medically significant infection	163 (31.7%)

OS at 6 months:

- Untreated set: 5.5% [1.1-15.6]
- Treated set: 83.7% [79.8-86.9]



Median FU: 8.1 months

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nature medicine

ARTICLES

https://doi.org/10.1038/s41591-022-01969-y

Check for updates

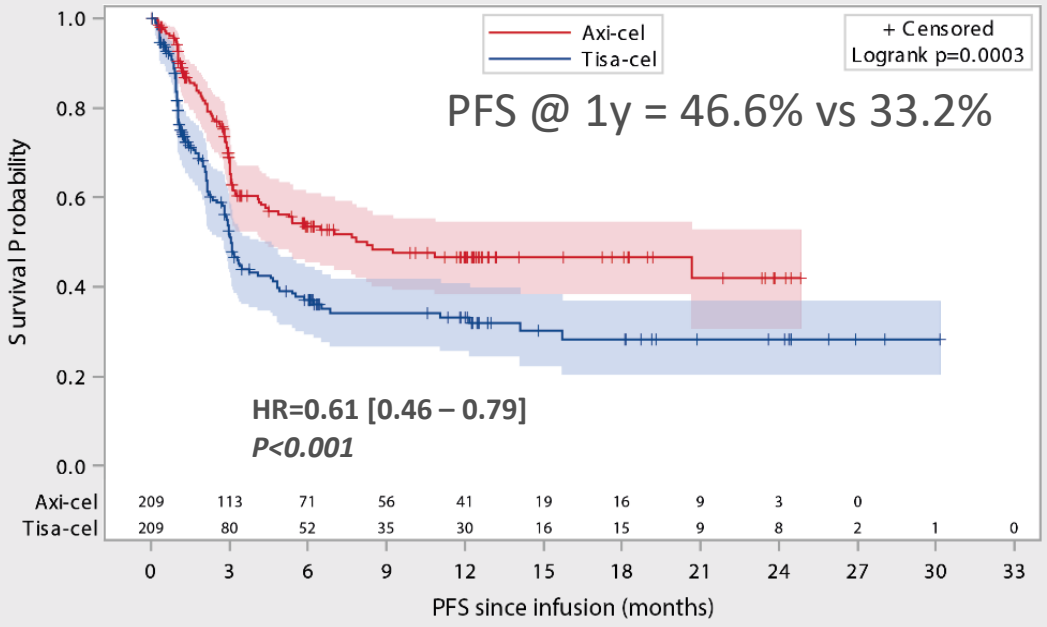
OPEN

A real-world comparison of tisagenlecleucel and axicabtagene ciloleucel CAR T cells in relapsed or refractory diffuse large B cell lymphoma

Emmanuel Bachy[1,2] ✉, Steven Le Gouill[3], Roberta Di Blasi[4], Pierre Sesques[1], Guillaume Manson[5], Guillaume Cartron[6], David Beauvais[7], Louise Roulin[8], François Xavier Gros[9], Marie Thérèse Rubio[10], Pierre Bories[11], Jacques Olivier Bay[12], Cristina Castilla Llorente[13], Sylvain Choquet[14], René-Olivier Casasnovas[15], Mohamad Mohty[16], Stéphanie Guidez[17], Magalie Joris[18], Michaël Loschi[19], Sylvain Carras[20], Julie Abraham[21], Adrien Chauchet[22], Laurianne Drieu La Rochelle[23], Bénédicte Deau-Fischer[24], Olivier Hermine[25], Thomas Gastinne[26], Jean Jacques Tudesq[6], Elodie Gat[27], Florence Broussais[28], Catherine Thieblemont[4], Roch Houot[5] and Franck Morschhauser[7,29]

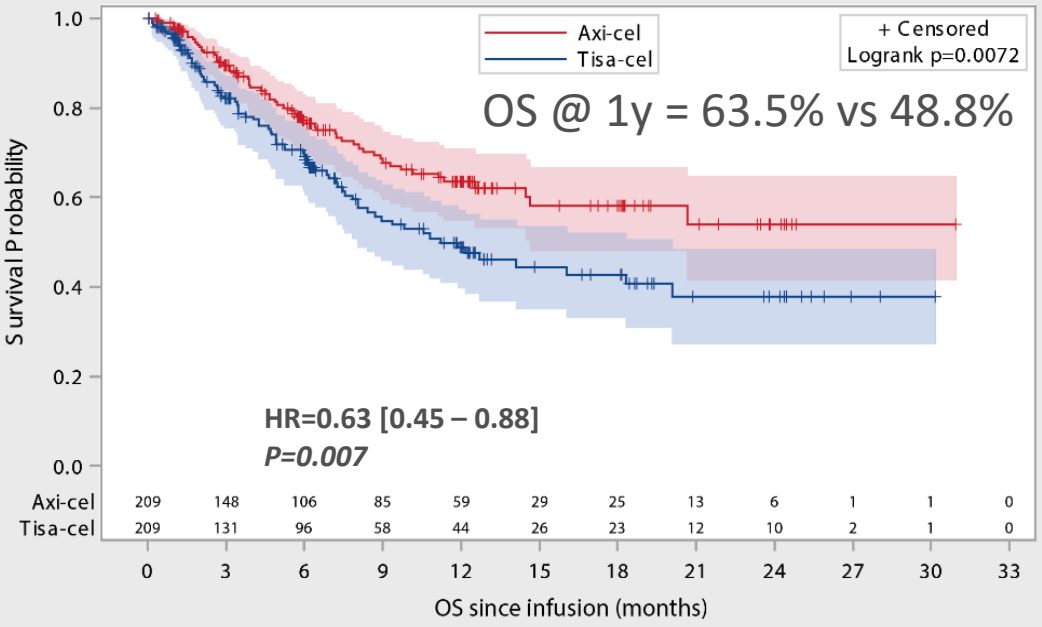
Axi-cel vs Tisa-cel : Efficacy

PFS



	No. of Subjects	Event	Censored	Median Survival (95%CL)
Axi-cel	209	43.1 % (90)	56.9 % (119)	8.2 (4.4 ; NA)
Tisa-cel	209	55.5 % (116)	44.5 % (93)	3.1 (2.8 ; 4.1)

OS



	No. of Subjects	Event	Censored	Median Survival (95%CL)
Axi-cel	209	28.2 % (59)	71.8 % (150)	Not reached (14.7 ; NA)
Tisa-cel	209	37.8 % (79)	62.2 % (130)	11.2 (8 ; 20.1)

Median follow-up = 11.7 months

Bachy et al., Nature Medicine 2022

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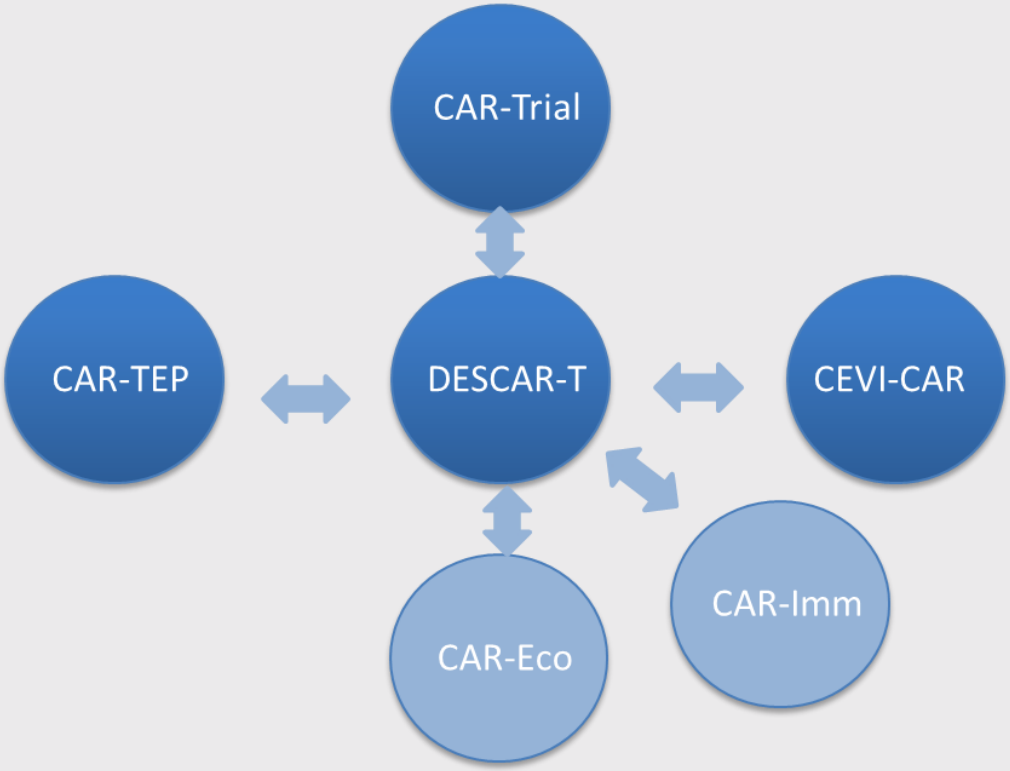
Conclusions about DESCAR-T registry

DESCAR-T Registry :

- Provides real-life data to clinicians, health authorities and all stakeholders
- One of the largest national CAR T-cell registry (≈2,000 pts in 3 years, >50 pts/month)
- Multi-tumor and multi-group registry (therapy-based)
- Collaboration between academic groups, health authorities, pharmaceutical companies
- Addresses several purposes:
  - CAR T-cells reimbursement
  - Real-life evaluation
  - Research

PERSPECTIVES

Backbone to build multi-modal network expertise (including immuno-monitoring, biobanking, imaging, health economy) in CAR T-cells (work in progress)



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CONCLUSIONS

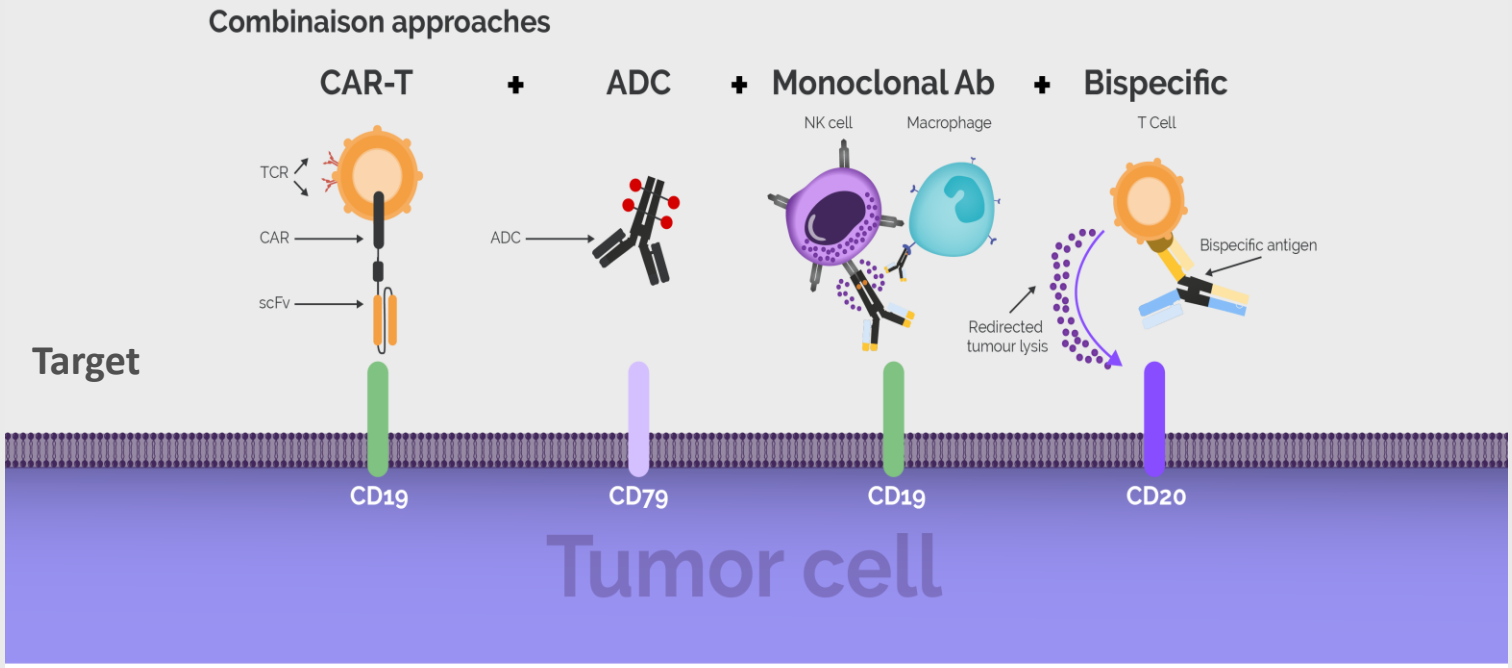
- CAR-T cells have confirmed their efficacy in real life in hematological malignancies (DLBCL ALL, myeloma, MCL, FL ..)
- CAR-T cells have opened the door to a large new therapeutic era: the cellular therapy era
- Major improvement in CARs design are on the tracks to enhance efficacy while reducing toxicities

QUESTIONS:

- Efficacy CAR-T in solid tumors ?
- Are CAR-T cells superior to bi- or tri- specific ?
- How to customize easy to use CARs in real life ?
- Are CARs therapies affordable ? Cost toxicities ?

Conclusions (2): combinaison approaches

Immunotherapy drugs



Anti-tumor cell toxicities

Direct apoptosis, Immune check points
ADCC, ADCP, Antitumor T-cell response

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