Place de l'aphérèse au regard des nouvelles thérapies cellulaires et géniques

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Received: 29 November 2022 | Revised: 25 January 2023 | Accepted: 27 January 2023
DOI: 10.1002/jca.22043

Journal of Clinical Apheresis ASFA WILEY

Guidelines on the Use of Therapeutic Apheresis in Clinical Practice – Evidence-Based Approach from the Writing Committee of the American Society for Apheresis: The Ninth Special Issue

Laura Connelly-Smith[1] | Caroline R. Alquist[2] | Nicole A. Aqui[3] | Jan C. Hofmann[4] | Reinhard Klingel[5,6] | Oluwatoyosi A. Onwuemene[7] | Christopher J. Patriquin[8] | Huy P. Pham[9] | Amber P. Sanchez[10] | Jennifer Schneiderman[11] | Volker Witt[12] | Nicole D. Zantek[13] | Nancy M. Dunbar[14]

TABLE 2 Category definitions for therapeutic apheresis

Category	Description
I	Disorders for which apheresis is accepted as first-line therapy, either as a primary standalone treatment or in conjunction with other modes of treatment.
II	Disorders for which apheresis is accepted as second-line therapy, either as a standalone treatment or in conjunction with other modes of treatment.
III	Optimum role of apheresis therapy is not established. Decision-making should be individualized.
IV	Disorders in which published evidence demonstrates or suggests apheresis to be ineffective or harmful. IRB/Ethics Committee approval is desirable if apheresis treatment is undertaken in these circumstances.

Abbreviation: IRB, Institutional Review Board.

Recommendation	Description	Methodological quality of supporting evidence	Implications
Grade 1A	Strong recommendation, high-quality evidence	RCTs without important limitations or overwhelming evidence from observational studies	Strong recommendation, can apply to most patients in most circumstances without reservation
Grade 1B	Strong recommendation, moderate quality evidence	RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies	Strong recommendation, can apply to most patients in most circumstances without reservation
Grade 1C	Strong recommendation, low-quality or very low-quality evidence	Observational studies or case series	Strong recommendation but may change when higher-quality evidence becomes available
Grade 2A	Weak recommendation, high-quality evidence	RCTs without important limitations or overwhelming evidence from observational studies	Weak recommendation, best action may differ depending on circumstances or patients' or societal values
Grade 2B	Weak recommendation, moderate-quality evidence	RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies	Weak recommendation, best action may differ depending on circumstances or patients' or societal values
Grade 2C	Weak recommendation, low-quality or very low-quality evidence	Observational studies or case series	Very weak recommendations; other alternatives may be equally reasonable

Abbreviation: RCT, randomized controlled trial.
Source: Adopted from References 1 and 2.

L’aphérèse thérapeutique en hématologie et oncologie

- Collecte de cellules mononucléées sanguines :
  - Autogreffes de cellules hématopoïétiques
  - Allogreffes de cellules hématopoïétiques
  - Prélèvement de cellules mononucléées sanguines autologues, destinées à initier la fabrication de médicaments de thérapies innovantes
- *Autres procédures:*
  - *Photochimiothérapie extracorporelle, protocoles de désensibilisation de receveurs allo-immunisés …*

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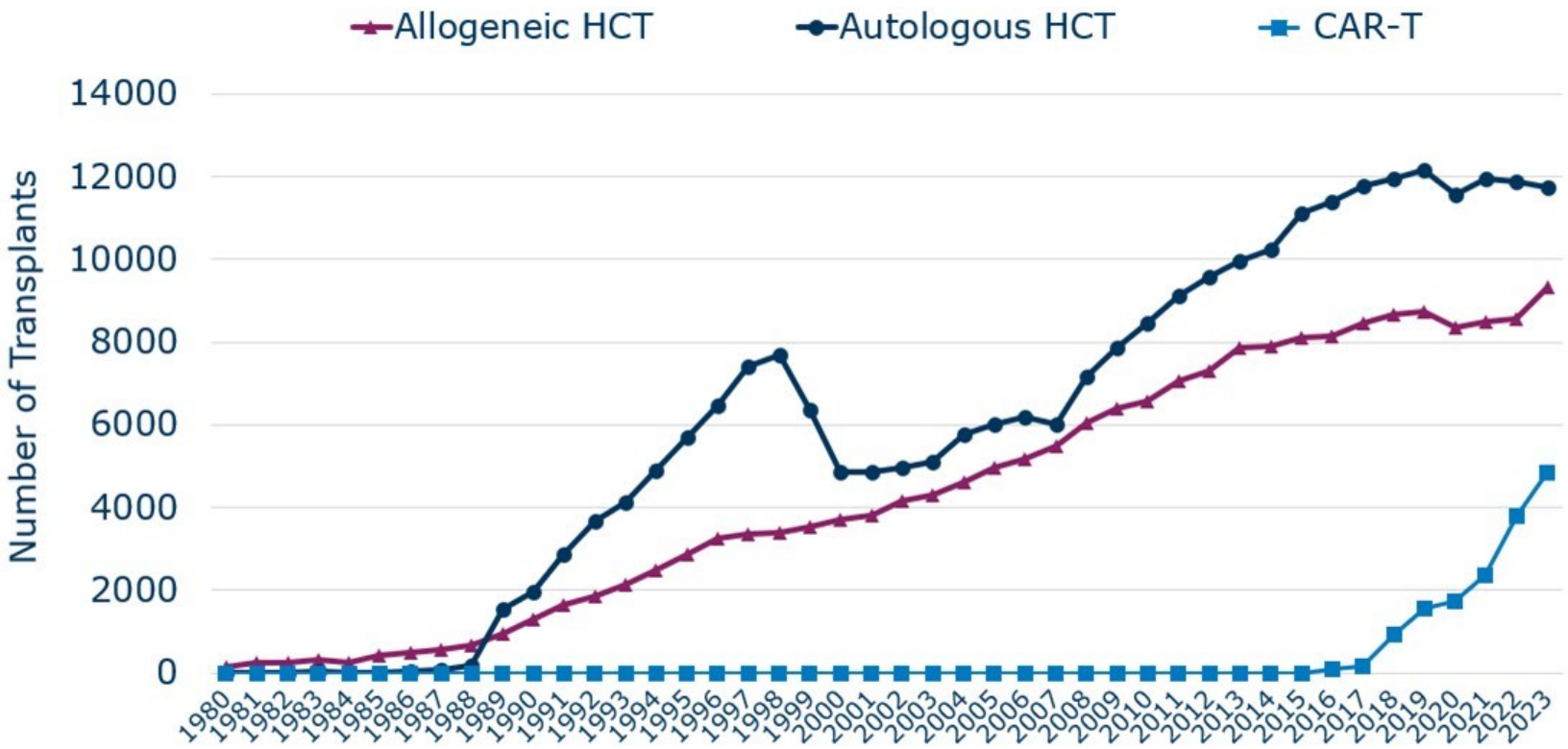
Transplantation, heart	Cellular rejection	ECP	II	1B	249
	Recurrent rejection	ECP	II	1B	
	Rejection prophylaxis	ECP	II	2A	
	Desensitization	TPE	II	1C	
	Rejection prophylaxis[a]	TPE	II	1C	
	Antibody mediated rejection	TPE	III	2C	
Transplantation, hemapoietic stem cell, ABO incompatible	Major ABO incompatible, HPC(M)	TPE	II	1B	251
	Major ABO incompatible, HPC(A)	TPE	II	2B	
	Minor ABO incompatible, HPC(A)	RBC exchange	III	2C	
	Pure red cell aplasia	TPE	III	2C	
Transplantation, hematopoietic stem cell, HLA desensitization		TPE	III	2C	253
Transplantation, intestine[a]	Antibody mediated rejection	TPE	III	2C	255
	Desensitization	TPE	III	2C	
Transplantation, kidney, ABO compatible	Antibody-mediated rejection	TPE/IA	I	1B	257
	Desensitization/prophylaxis, living donor	TPE/IA	I	1B	
Transplantation, kidney, ABO incompatible	Desensitization, living donor	TPE/IA	I	1B	259
	Antibody mediated rejection	TPE/IA	II	1B	
Transplantation, liver	Desensitization, ABOi, living donor	TPE	I	1C	261
	Desensitization, ABOi, deceased donor	TPE	III	2C	

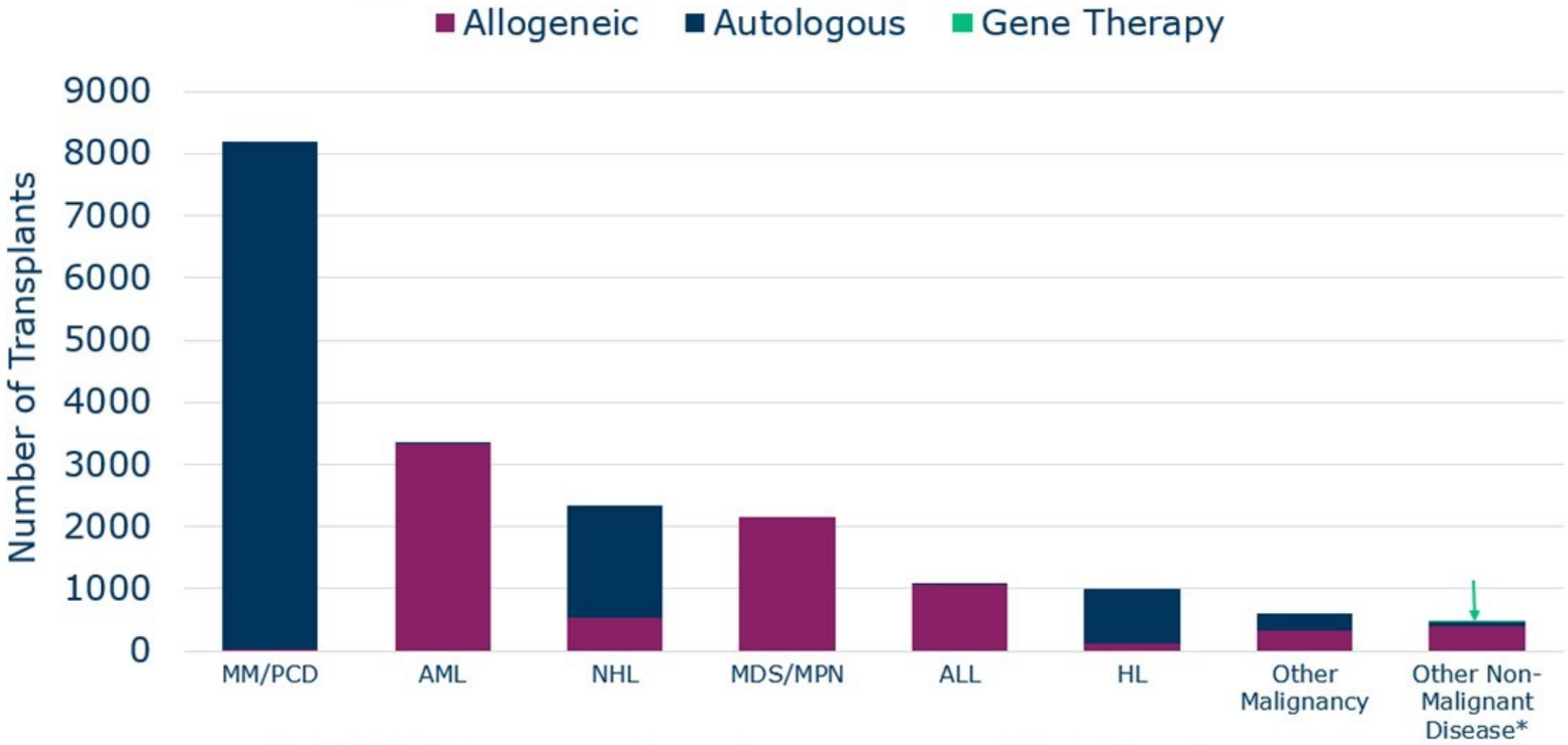
L’aphérèse thérapeutique en hématologie et oncologie

- Collecte de cellules mononucléées sanguines :
  - Autogreffes de cellules hématopoïétiques
  - Allogreffes de cellules hématopoïétiques
  - Prélèvement de cellules mononucléées sanguines autologues, destinées à initier la fabrication de médicaments de thérapies innovantes
- *Autres procédures:*
  - *Photochimiothérapie extracorporelle, protocoles de désensibilisation de receveurs allo-immunisés …*

Number of 1st Cellular Therapies Reported to CIBMTR in the US



Number of HCTs by Indications in the US, 2023, Adult



*Includes 22 limited gene therapy events

Abbreviations:
ALL, acute lymphoblastic leukemia;
AML, acute myeloid leukemia;
CLL, chronic lymphocytic leukemia;
HL, Hodgkin lymphoma;
MDS, myelodysplastic syndromes;
MM, multiple myeloma;
MPN, myeloproliferative neoplasms;
NHL, non-Hodgkin lymphoma;
PCD, plasma cell disorders.

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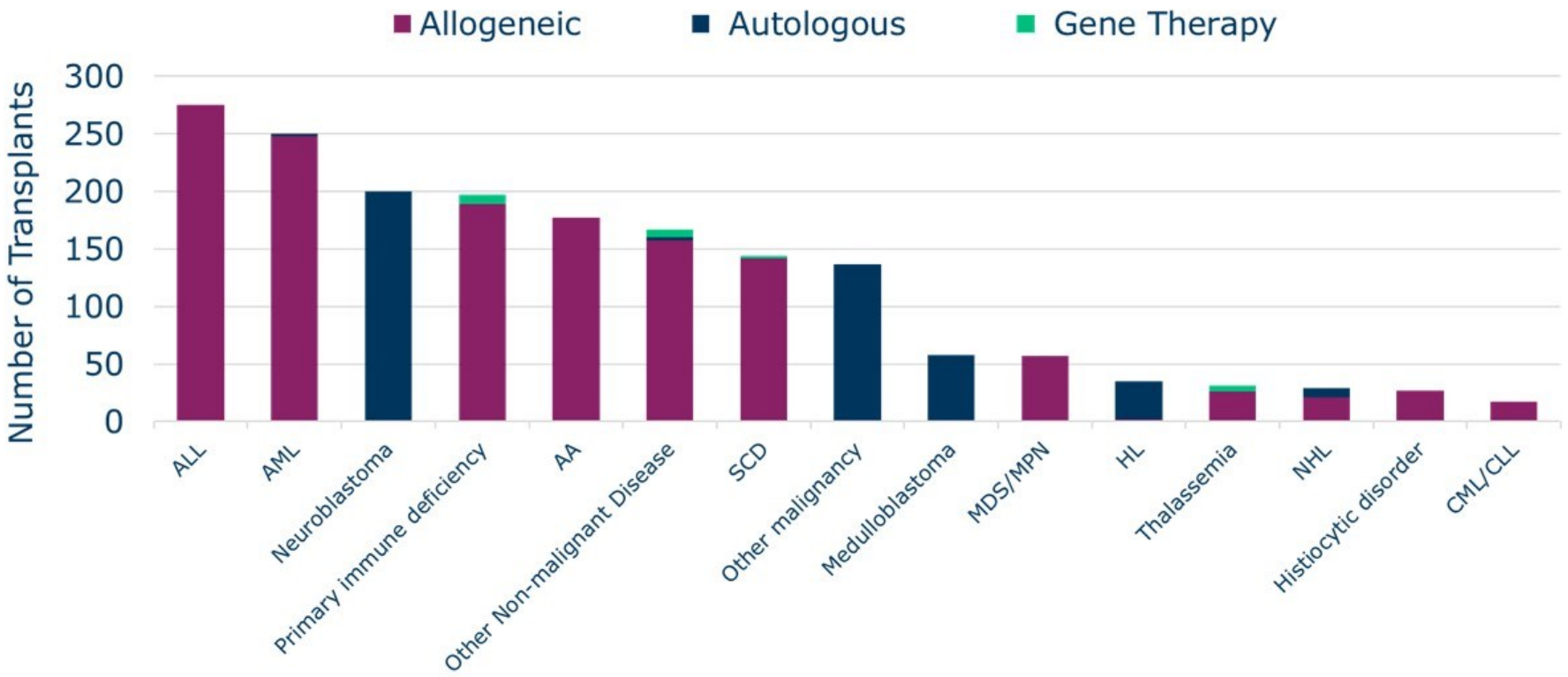
Number of HCTs by Indications in the US, 2023, Pediatrics



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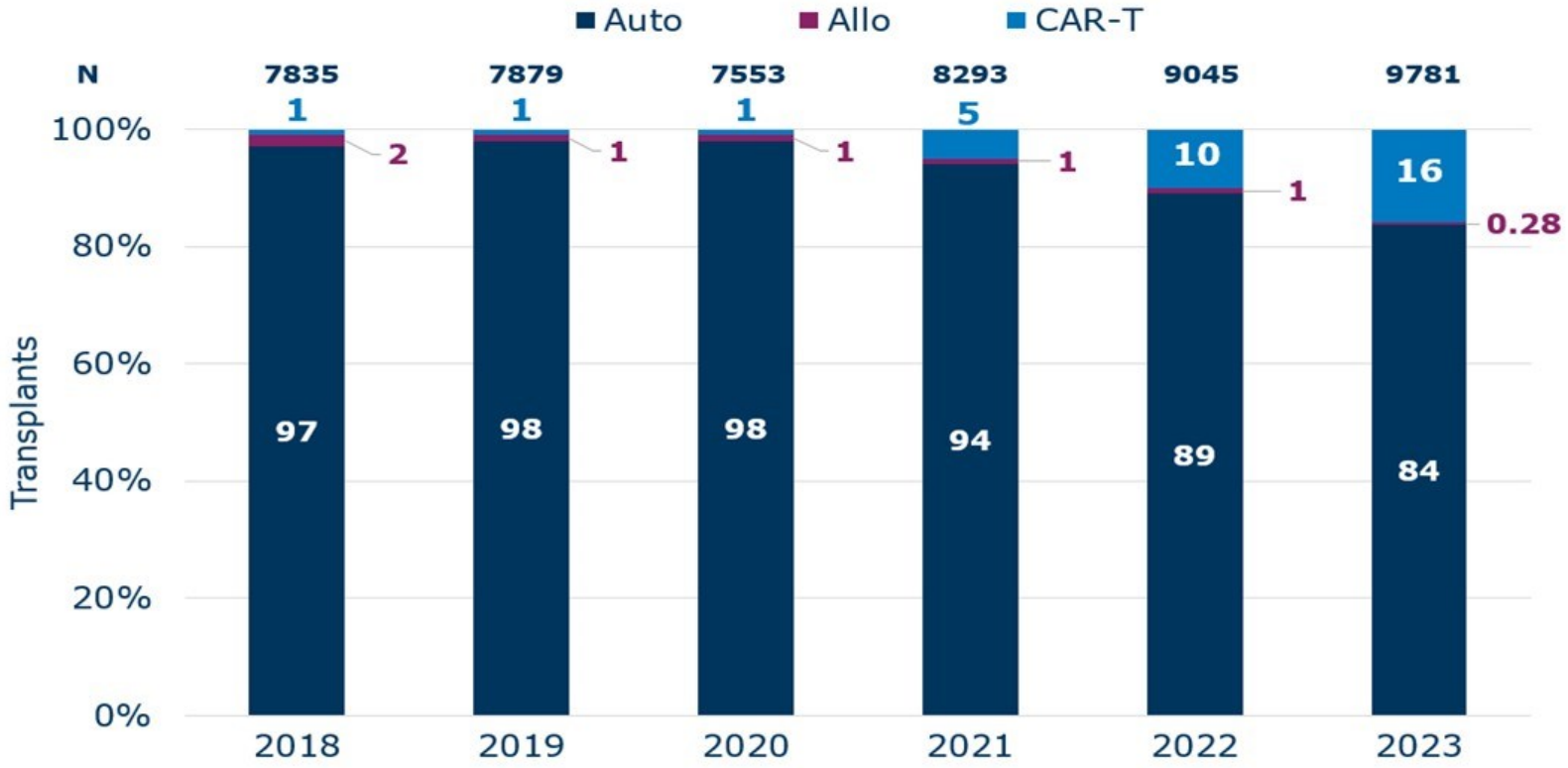
MPN, myeloproliferative neoplasms;
NHL, non-Hodgkin lymphoma;
SCD, sickle cell disease.

Autogreffes de cellules hématopoïétiques

- Myélomes multiples en 1° ligne thérapeutique
- Lymphomes malins non Hodgkiniens en rechute ou réfractaires
  - Lymphomes B diffus à grandes cellules (DLBCL)
  - Lymphomes T
  - Lymphomes cérébraux primitifs
- Autres

Relative Proportion of Multiple Myeloma Treatment by Type in the US



Abbreviations: allo, allogeneic; auto, autologous; CAR-T, chimeric antigen receptor T cell.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

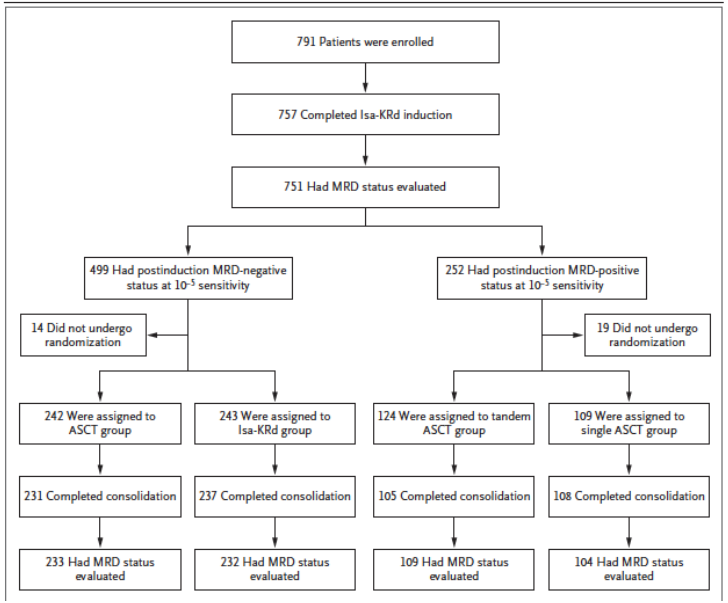
Measurable Residual Disease–Guided Therapy in Newly Diagnosed Myeloma

A. Perrot,[1] J. Lambert,[2] C. Hulin,[3] A. Pieragostini,[4] L. Karlin,[5] B. Arnulf,[6] P. Rey,[7] L. Garderet,[8] M. Macro,[9] M. Escoffre-Barbe,[10] J. Gay,[11] T. Chalopin,[12] R. Gounot,[13] J.-M. Schiano,[14] M. Mohty,[15] X. Leleu,[16] S. Manier,[17] C. Mariette,[18] C. Chaleteix,[19] T. Braun,[20] B. De Prijck,[21] H. Avet-Loiseau,[22] J.-Y. Mary,[2] J. Corre,[22] P. Moreau,[23] and C. Touzeau,[23] for the MIDAS Study Group*

*A complete list of the investigators in the MIDAS trial is provided in the Supplementary Appendix, available at NEJM.org.

This article was published on June 3, 2025, at NEJM.org.

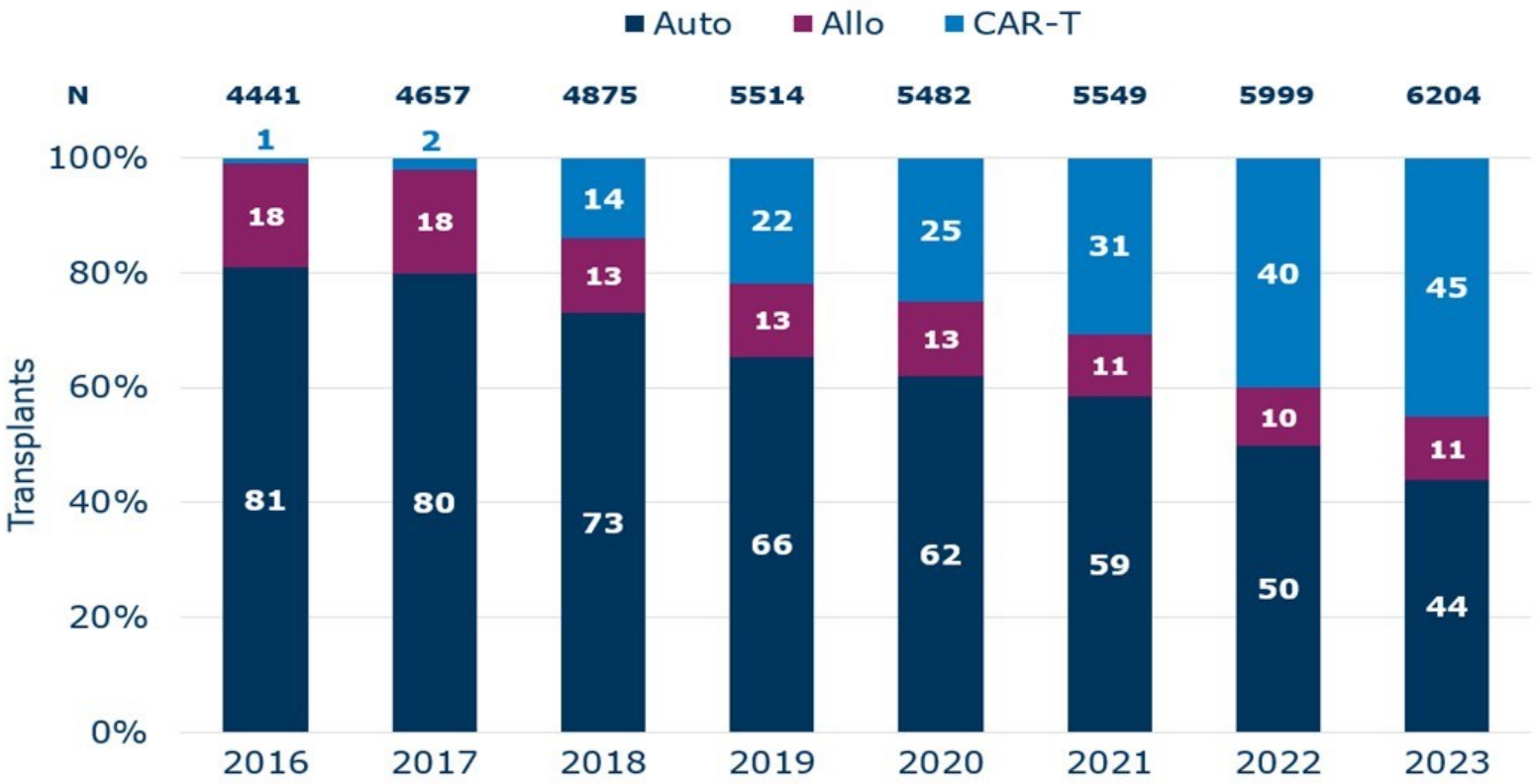
DOI: 10.1056/NEJMoa2505133



CONCLUSIONS

Among patients who were MRD-negative at 10^{-5} sensitivity after induction, the percentage with a premaintenance MRD-negative status at 10^{-6} sensitivity was not significantly higher with ASCT than with Isa-KRd. Among patients who were MRD-positive status at 10^{-5} sensitivity after induction, the percentage with a premaintenance MRD-negative status at 10^{-6} sensitivity was not significantly higher with tandem ASCT than with single ASCT. (Funded by Intergroupe Francophone du Myélome and others; MIDAS ClinicalTrials.gov number, NCT04934475.)

Relative Proportion of Lymphoma Treatment by Type in the US



Abbreviations: allo, allogeneic; auto, autologous; CAR-T, chimeric antigen receptor T cell.

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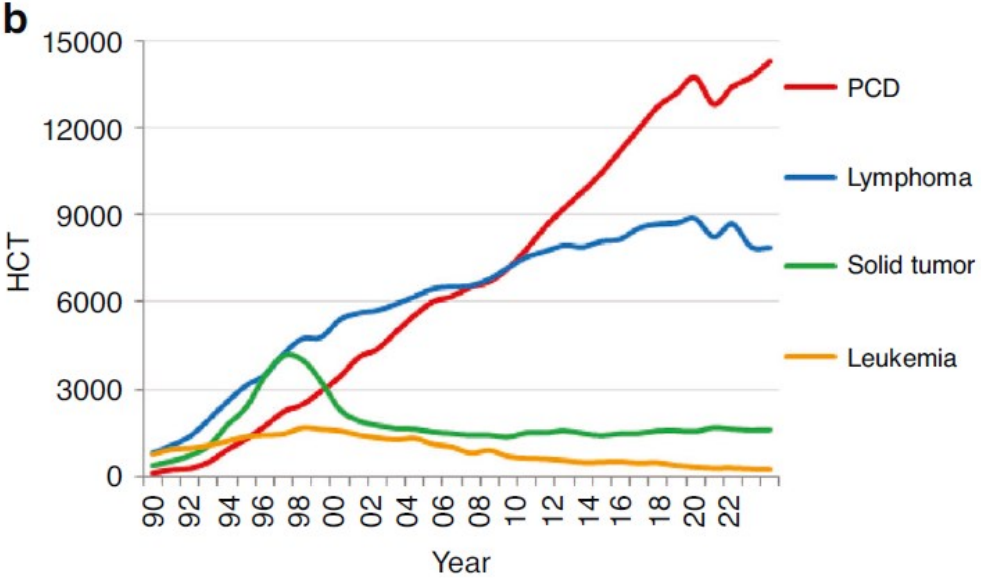
ARTICLE OPEN

The 2023 EBMT report on hematopoietic cell transplantation and cellular therapies. Increased use of allogeneic HCT for myeloid malignancies and of CAR-T at the expense of autologous HCT

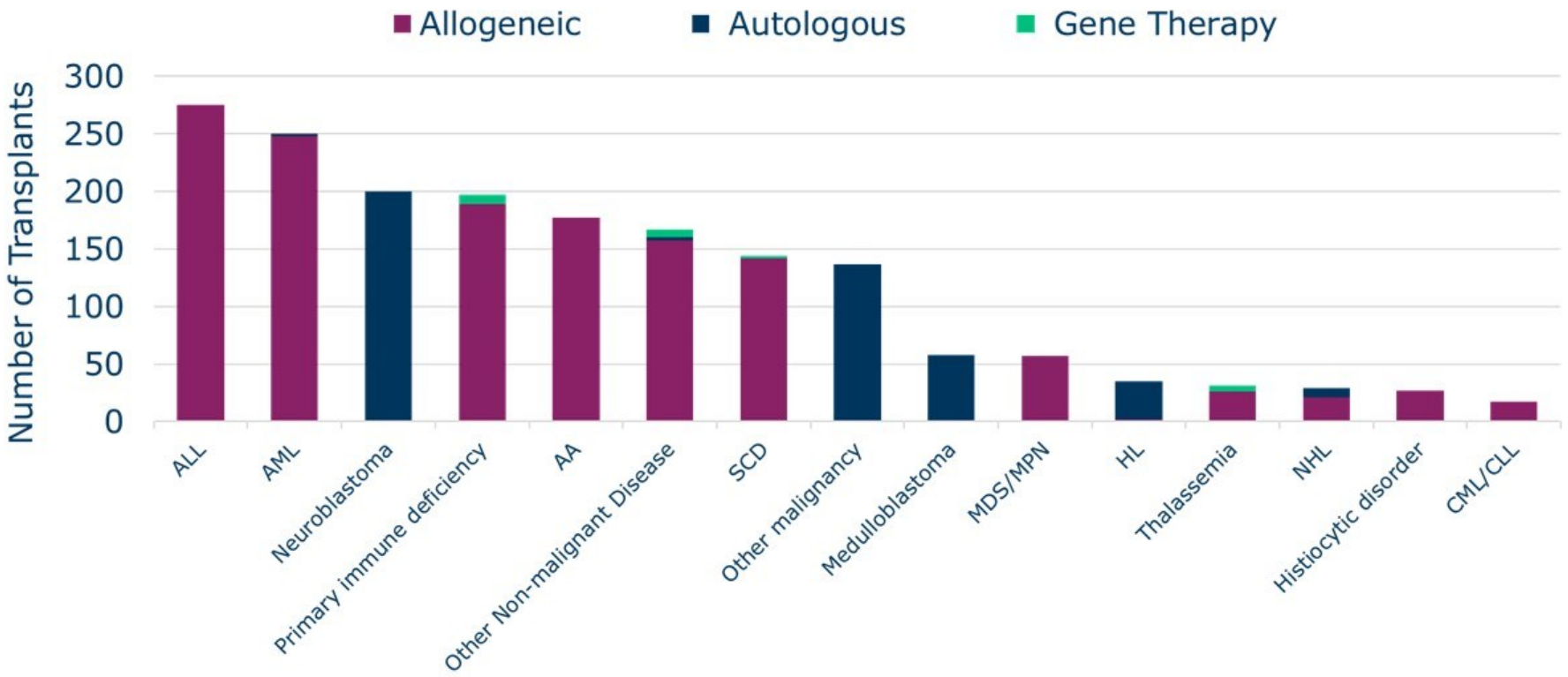
Jakob R. Passweg[1], Helen Baldomero[1,✉], Marina Atšja[2], Iliana Kleovoulou[2], Aleksandra Witaszek[2], Tobias Alexander[3], Emanuele Angelucci[4], Dina Averbuch[5], Ali Bazarbachi[6], Fabio Ciceri[7], Raffaella Greco[7], Mette D. Hazenberg[8,9], Krzysztof Kalwak[10], Donal P. McLornan[11], Bénédicte Neven[12], Zinaida Perić[13], Antonio M. Risitano[14], Annalisa Ruggeri[7], Isabel Sánchez-Ortega[15], John A. Snowden[16] and Anna Sureda[17]



Allogreffes de cellules hématopoïétiques

- Hémopathies malignes myéloïdes (LAM, SMD, SMP)
- Hémopathies malignes lymphoïdes (LAL, *LMNH B ou T*)
- Affections non malignes affectant la production ou la fonction d'un ou plusieurs lignages hématopoïétiques
  - Aplasies médullaires
  - Hémoglobinopathies
  - Déficits immunitaires

Number of HCTs by Indications in the US, 2023, Pediatrics



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Abbreviations:
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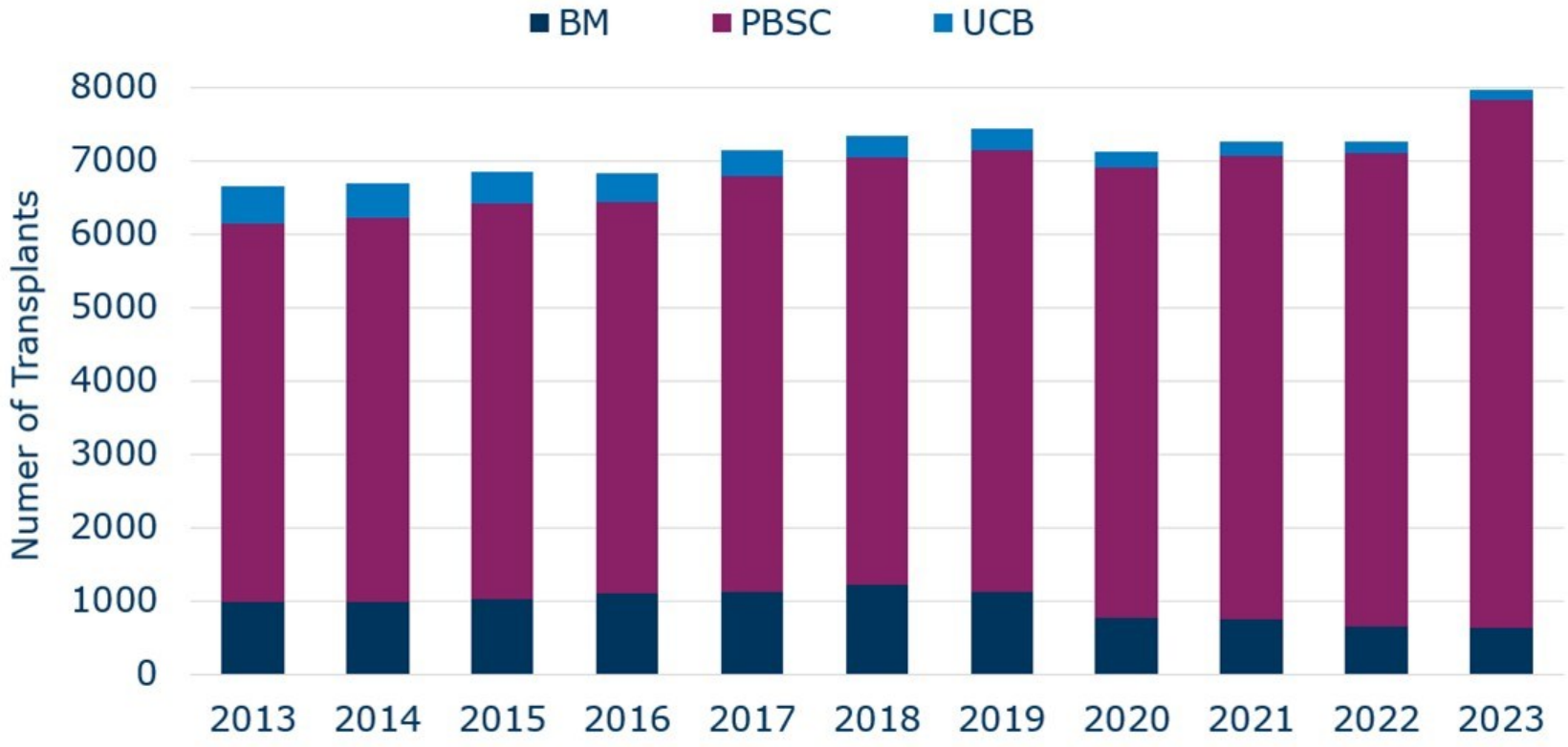
AA, aplastic anemia;
CLL, chronic lymphocytic leukemia;
CML, chronic myeloid leukemia;
HL, Hodgkin lymphoma;
MDS, myelodysplastic syndromes;
MPN, myeloproliferative neoplasms;
NHL, non-Hodgkin lymphoma;
SCD, sickle cell disease.

Number of Allogeneic HCTs in the US by Graft Source, Adults



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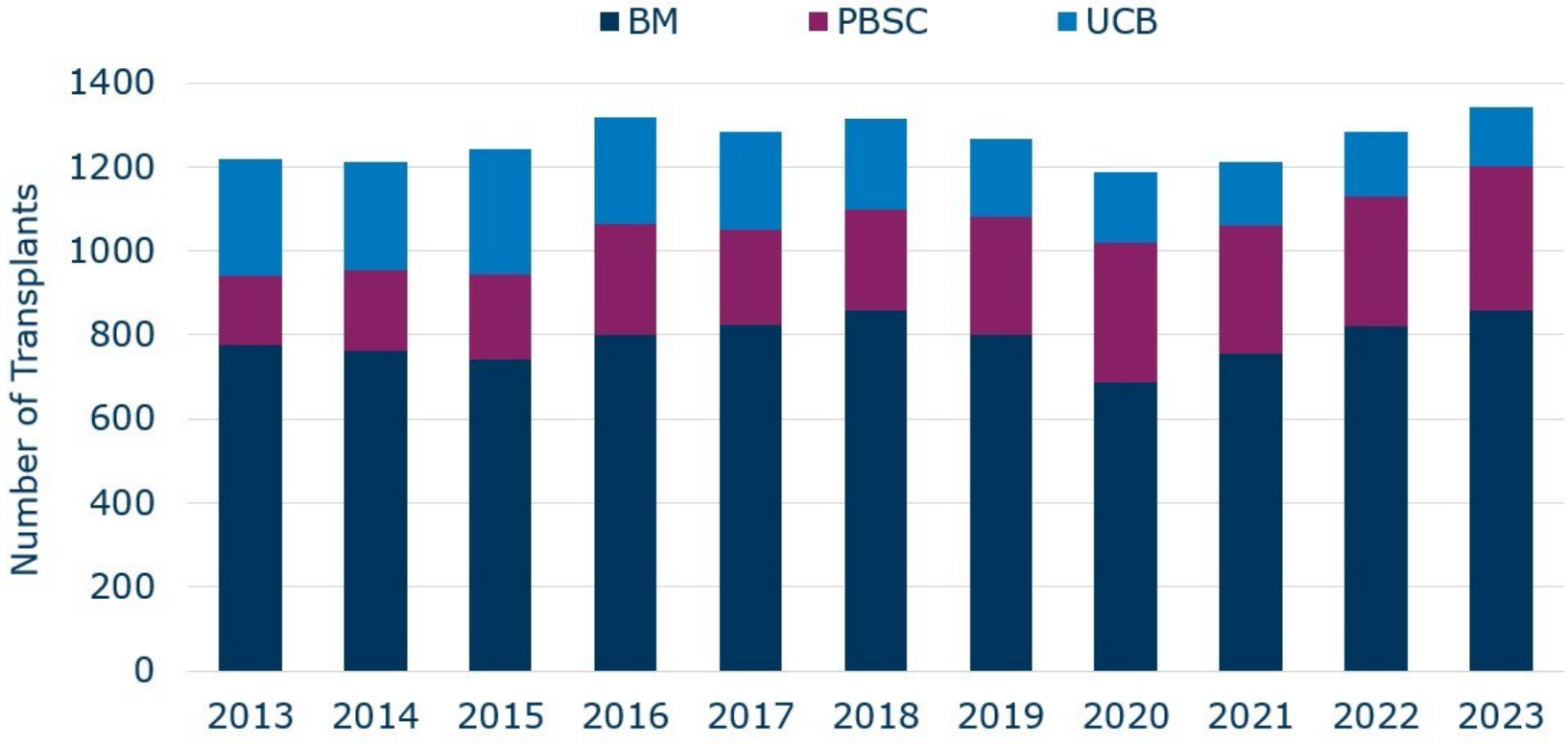
Abbreviations: BM, bone marrow; PBSC, peripheral blood stem cells; UCB, umbilical cord blood.

Number of Allogeneic HCTs in the US by Graft Source, Pediatrics



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Abbreviations: BM, bone marrow; PBSC, peripheral blood stem cells; UCB, umbilical cord blood.

Allogreffes de cellules hématopoïétiques

- Prélèvements de cellules souches sanguines, chez un donneur ayant reçu un traitement de mobilisation (des cellules souches hématopoïétiques …; rhG-CSF)
- Prélèvements de cellules mononucléées sanguines allogéniques, en vue de préparer des doses de « lymphocytes du donneur » (DLI, « Donor Lymphocyte Infusion »)

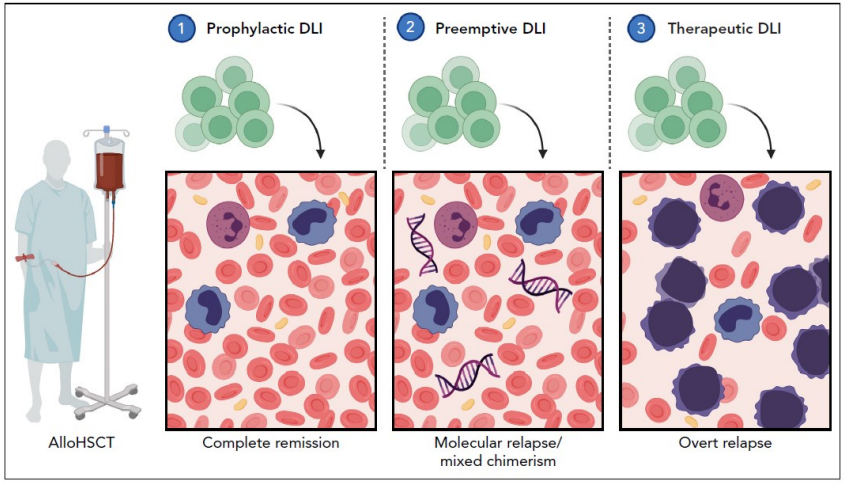

Figure 1. Overview of different strategies to administer DLI. (1) Prophylactic DLI is administered after a defined interval posttransplant to reduce the risk of relapse. (2) Preemptive DLI serves to restore GvL on impending relapse as detected by persisting MRD or LOC. (3) Therapeutic DLI is administered to treat overt hematologic relapse. Abbreviations: DLI, donor lymphocyte infusion; GvL, graft-versus-leukemia effect; LOC, loss of complete donor chimerism; MRD, measurable residual disease. Image created in BioRender.

How I treat high-risk acute myeloid leukemia using preemptive adoptive cellular immunotherapy

Alexander Biederstädt[1,2] and Katayoun Rezvani[1]

[1]Department of Stem Cell Transplantation and Cellular Therapy, The University of Texas MD Anderson Cancer Center, Houston, TX; and [2]Department of Medicine III: Hematology and Oncology, School of Medicine, Technical University of Munich, Munich, Germany

22 blood® 5 JANUARY 2023 | VOLUME 141, NUMBER 1

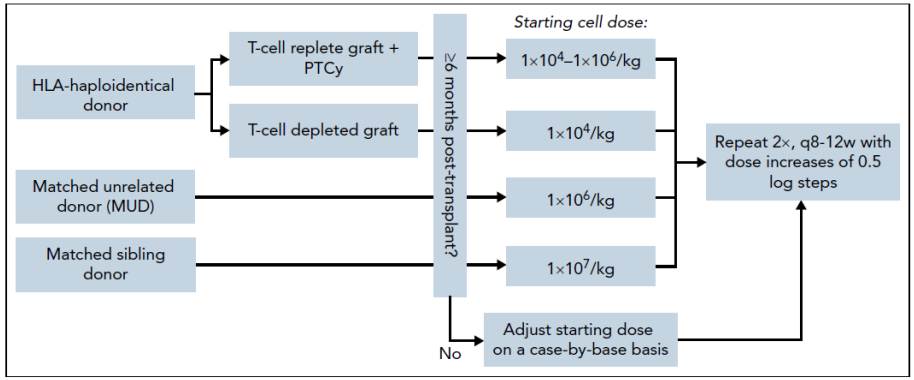

Figure 4. MD Anderson Cancer Center institutional guidelines for DLI starting dose. DLI starting dose should be selected based on donor and graft type. If DLI is administered earlier than 6 months after transplant, the starting cell dose should be adjusted on a case-by-case basis to minimize the risk of GvHD. DLI is repeated every alternating cycle of HMA therapy, escalating cell doses incrementally in 0.5 log steps. q, every; w, weeks.

Bull Cancer 2019; 106S: S35-S39
en ligne sur / on line on
www.em-consulte.com/revue/bulcan
www.sciencedirect.com

Injections de lymphocytes du donneur (DLI) : recommandations de la Société francophone de greffe de moelle et de thérapie cellulaire (SFGM-TC)

John De Vos [1], Etienne Baudoux [2], Jacques-Olivier Bay [3], Boris Calmels [4], Audrey Cras [5], Jean El Cheikh [6], Marie-Agnès Guerout-Verite [7], Marie-Noëlle Lacassagne [8], Sylvain Lamure [9], Catherine Letellier [10], Anne-Lise Menard [11], Etienne Daguindau [12], Xavier Poiré [13], Ibrahim Yakoub-Agha [14,15], Thierry Guillaume [16]

TABLEAU I
Doses de DLI préconisées (CD3/kg du receveur)

Type de donneur	DLI en escalade	Rechute franche	Préemptif Mrd+ et/ou chimérisme partiel (<95 %)	Prophylactique
Géno ou phéno 10/10	1e DLI	1×10^7	5×10^6	1×10^6
	2e DLI	5×10^7	1×10^7	5×10^6
	3e DLI	1×10^8	5×10^7	1×10^7
Phéno 9/10	1e DLI	$1–5 \times 10^6$	1×10^6	$0,5–1 \times 10^6$
	2e DLI	$0,5–1 \times 10^7$	5×10^6	$1–5 \times 10^6$
	3e DLI	$0,1–1 \times 10^8$	1×10^7	$0,5–1 \times 10^7$
Haplo	1e DLI	$0,5–1 \times 10^6$	1×10^5	1×10^{51}
	2e DLI	$1–5 \times 10^6$	5×10^5	5×10^{51}
	3e DLI	1×10^7	1×10^6	1×10^{61}

[1]Il n'existe pas, au moment de la rédaction de ces recommandations, de publication relative à l'utilisation de DLI à titre prophylactique en situation haplo-identique. En conséquence, la prudence est de mise quant à leur utilisation dans cette situation.

SPECIAL SERIES: IMMUNOTHERAPY FOR HEMATOLOGICAL MALIGNANCIES

Defining the Role of Donor Lymphocyte Infusion High-Risk Hematologic Malignancies

Christoph Schmid, MD[1]; Jürgen Kuball, MD[2]; and Gesine Bug, MD[3]

Accepted on September 9, 2020 and published at ascopubs.org/journal/jco on January 12, 2021: DOI https://doi.org/10.1200/JCO.20.01719

TABLE 3. Timing and Dosing of Unmodified DLI in Relation to Indication and Donor Type Modified from Frederik Falkenburg et al[34]

Indication	Time After Allo-SCT (months)	Initial Cell Dose: MFD/MUD/mMUD Donor (CD3+ T cells/kg)	Initial Cell Dose: Haploidentical Donor (CD3+ T cells/kg)[a]
Prophylactic	3-6	1×10^5	Not recommended
Preemptive (MRD+)	3-6	1×10^5	Under discussion
Preemptive (MRD+)	≥ 6	1×10^6	1×10^4-1×10^5
Preemptive (incomplete or declining chimerism)[b]	3-6	1×10^5	Under discussion
Preemptive (incomplete or declining chimerism)[b]	≥ 6	1×10^6	1×10^4
Molecular relapse	3-6	1×10^5	Under discussion
Molecular relapse	≥ 6	1×10^6	1×10^4-1×10^5
Hematologic relapse (usually after disease control by pharmacotherapy)[d]	≥ 6[c]	1×10^7 (in case of lack of response after 4 weeks, 1×10^8)	3×10^5 (in case of lack of response after 4-6 weeks, 1×10^6)

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ARTICLE OPEN

Check for updates

Hematopoietic cell transplantation and cellular therapies in Europe 2022. CAR-T activity continues to grow; transplant activity has slowed: a report from the EBMT

Jakob R. Passweg[1], Helen Baldomero[1✉], Fabio Ciceri[2], Rafael de la Cámara[3], Bertram Glass[4], Raffaella Greco[2], Mette D. Hazenberg[5], Krzysztof Kalwak[6], Donal P. McLornan[7], Bénédicte Neven[8], Zinaida Perić[9], Antonio M. Risitano[10], Annalisa Ruggeri[2], John A. Snowden[11] and Anna Sureda[12]

Table 2. Numbers of patients treated with non-HC

Number of patients	DLI	CART		MSC	
		Allo	Auto	Allo	Auto
GvHD				273	1
Graft enhancement				30	
Autoimmune dis.			9	11	3
Genetic disease					
Infection				1	8
Malignancy - ALL		44	336		
Malignancy - HL/NHL		1	2258		
Malignancy - Myeloma		3	467		
Any other indication		4	83	15	13
DLI for graft enhancement/ failure	804				
DLI for residual disease	393				
DLI for relapse	1294				
DLI per protocol	363				
Total	**2854**	**52**	**3153**	**330**	**25**

The bold text indicates the subtotals of the data listed

Bone Marrow Transplantation (2021) 56:1651–1664
https://doi.org/10.1038/s41409-021-01227-8

EBMT

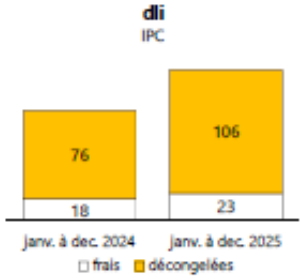
ARTICLE

Check for updates

Hematopoietic cell transplantation and cellular therapy survey of the EBMT: monitoring of activities and trends over 30 years

Jakob R. Passweg[1] · Helen Baldomero[1] · Christian Chabannon[2] · Grzegorz W. Basak[3] · Rafael de la Cámara[4] · Selim Corbacioglu[5] · Harry Dolstra[6] · Rafael Duarte[7] · Bertram Glass[8] · Raffaella Greco[9] · Arjan C. Lankester[10] · Mohamad Mohty[11] · Régis Peffault de Latour[12] · John A. Snowden[13] · Ibrahim Yakoub-Agha[14] · Nicolaus Kröger[15] · for the European Society for Blood and Marrow Transplantation (EBMT)

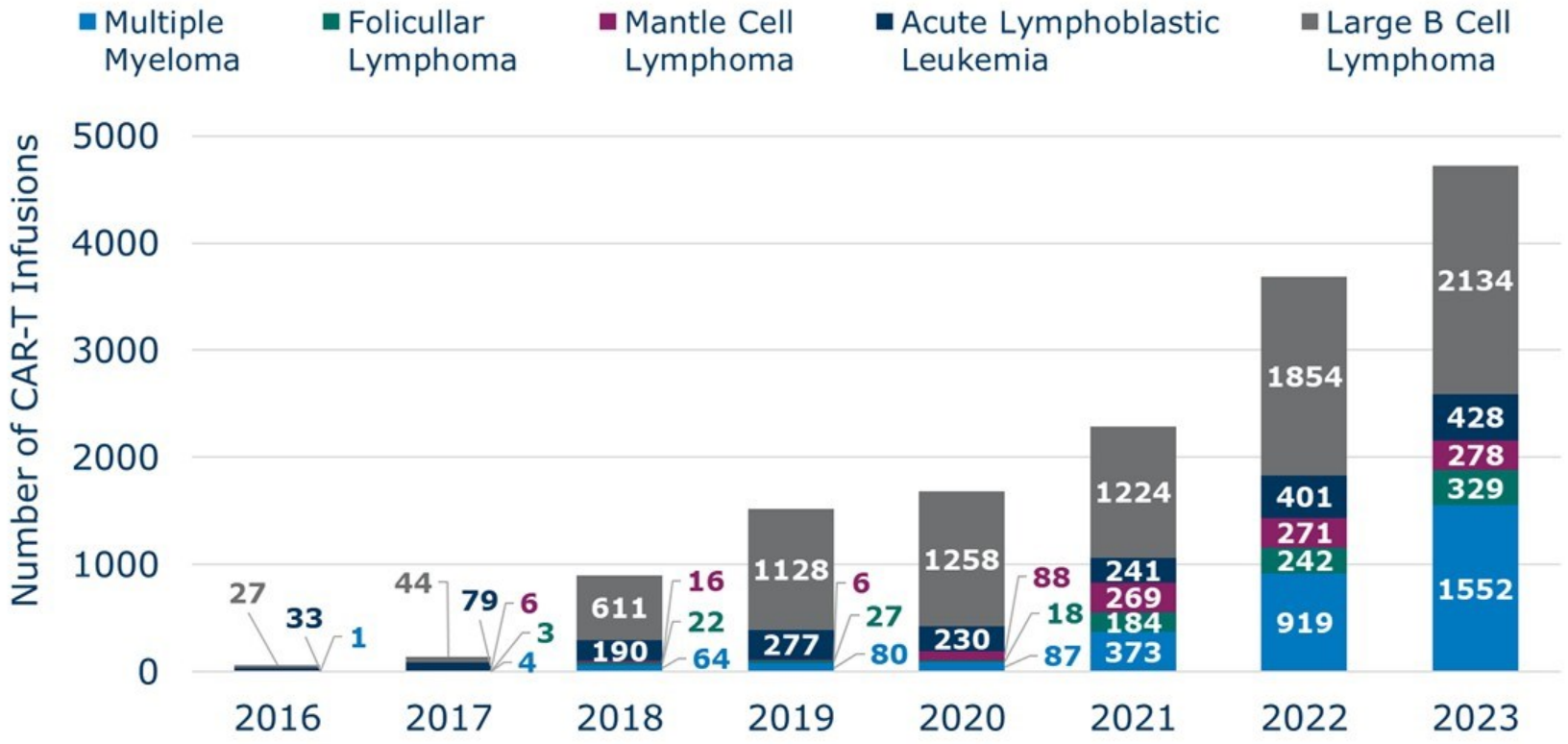
DLI for graft enhancement/failure	716
DLI for residual disease	431
DLI for relapse	1461
DLI per protocol	420
Total	**3028**



Production de médicaments de thérapies innovantes

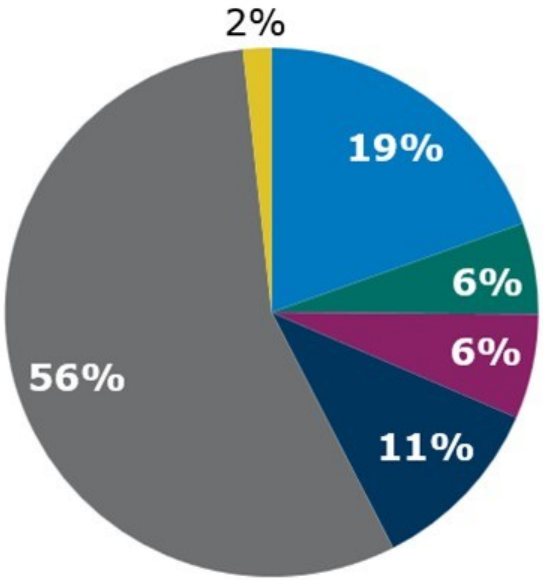
- Médicaments de thérapies géniques
  - Obtenus moyennant la modification génétique d'effecteurs immuns : lymphocytes T pour les CAR-T Cells autorisés et commercialisés, autres populations immunes pour de multiples médicaments en développement
  - Obtenus moyennant la modification génétique de cellules souches hématopoïétiques sanguines (CD34+)

Number of CAR-T Infusions by Indication in the US Annually

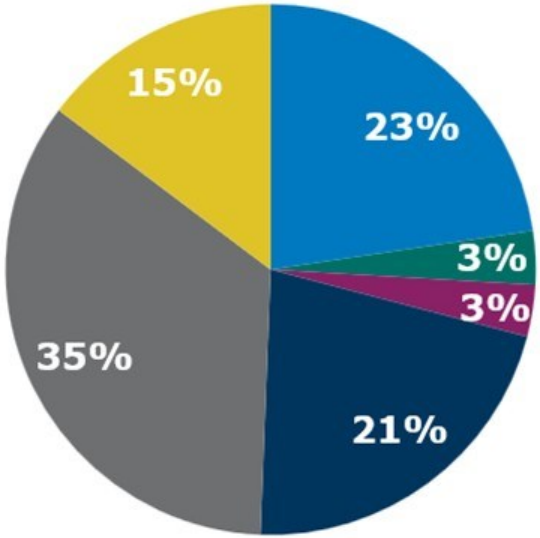


CAR-T indications 2016-2023

Commercial CAR-T Cells



Non-Commercial CAR-T Cells



- Multiple Myeloma
- Follicular Lymphoma
- Mantle Cell Lymphoma
- Acute Lymphoblastic Leukemia
- Large B Cell Lymphoma
- Other

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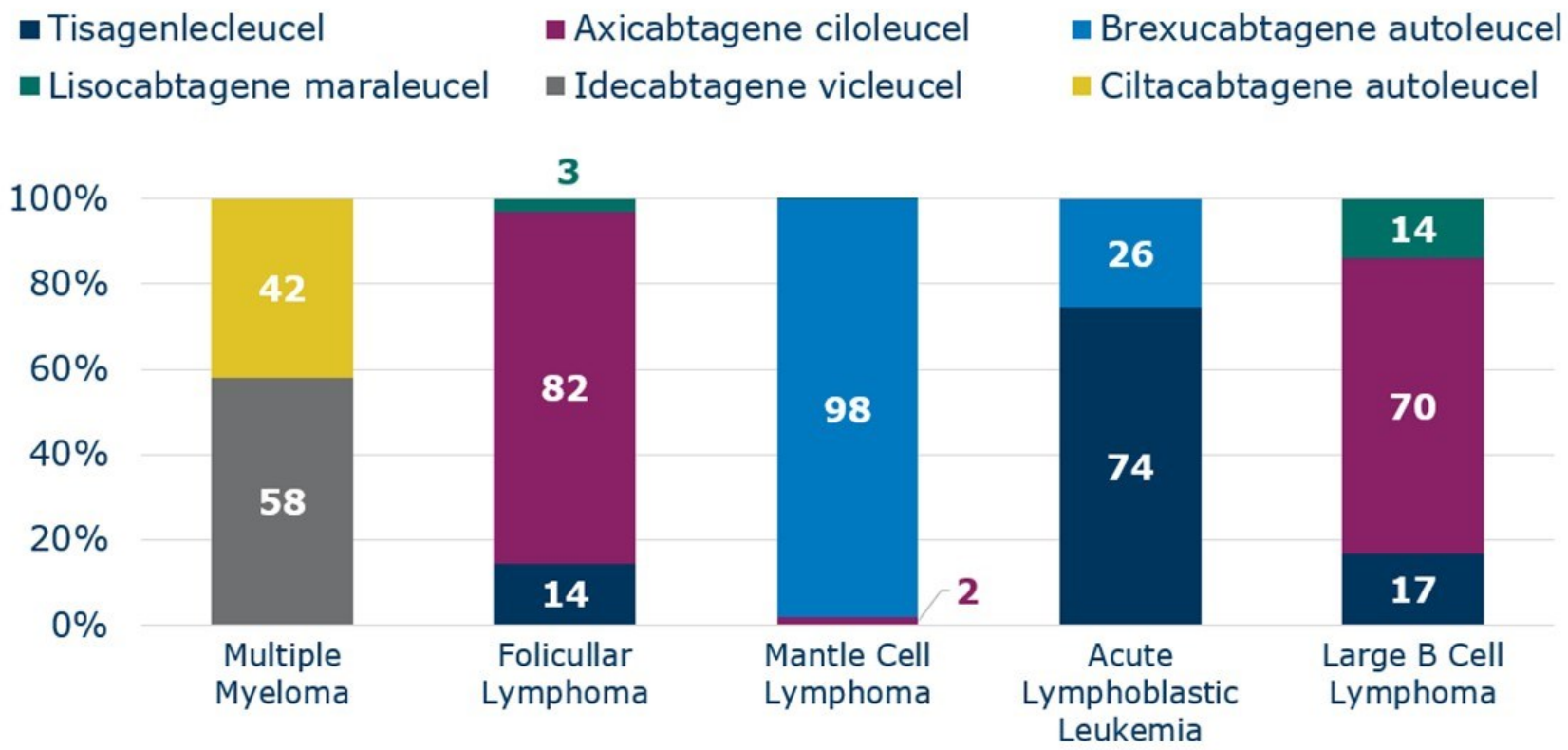
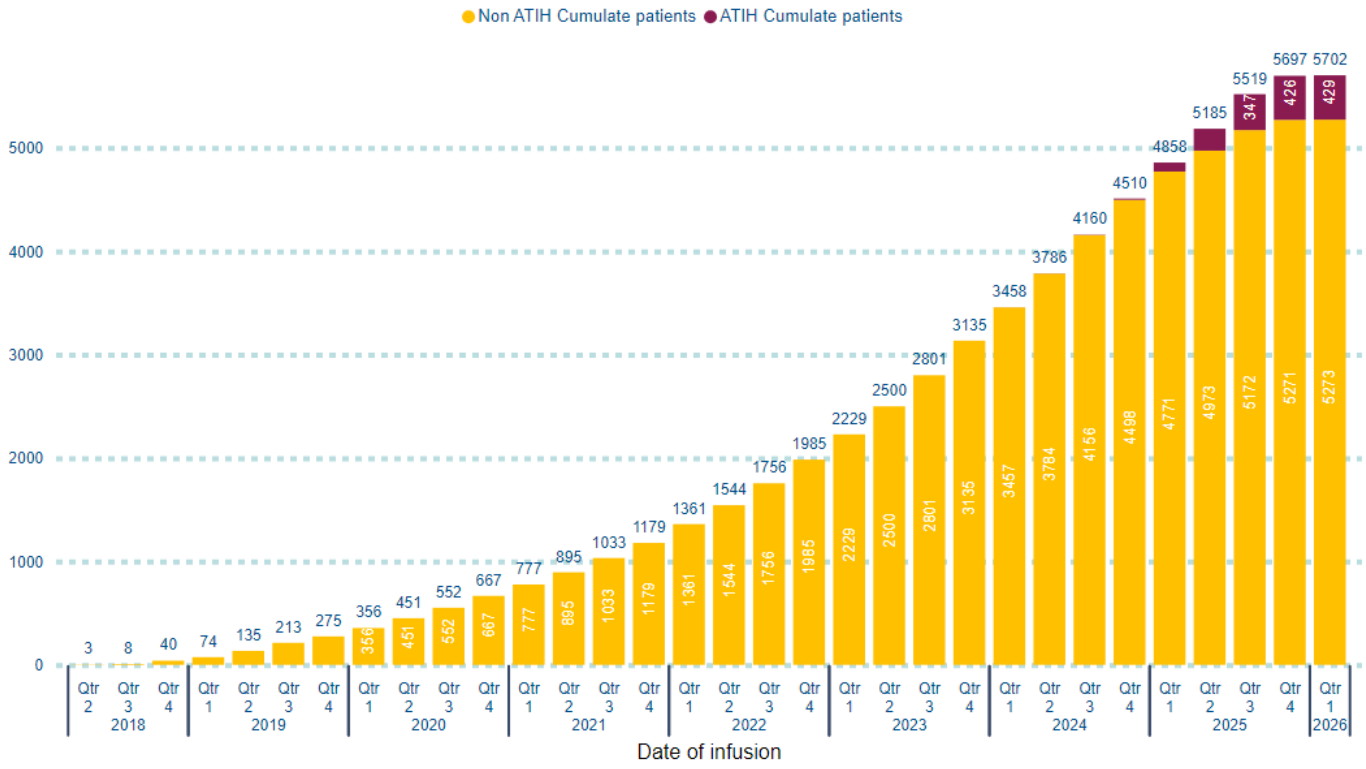
Infusions with Commercial CAR-T Cell Products in the US, 2016-2023



CIBMTR
A RESEARCH COLLABORATION BETWEEN THE MEDICAL COLLEGE OF WISCONSIN AND NMDP

Le registre Français DESCART



EBMT www.nature.com/bmt

ARTICLE OPEN

The 2023 EBMT report on hematopoietic cell transplantation and cellular therapies. Increased use of allogeneic HCT for myeloid malignancies and of CAR-T at the expense of autologous HCT

Jakob R. Passweg[1], Helen Baldomero[1,✉], Marina Atšja[2], Iliana Kleovoulou[2], Aleksandra Witaszek[2], Tobias Alexander[3], Emanuele Angelucci[4], Dina Averbuch[5], Ali Bazarbachi[6], Fabio Ciceri[7], Raffaella Greco[7], Mette D. Hazenberg[8,9], Krzysztof Kalwak[10], Donal P. McLornan[11], Bénédicte Neven[12], Zinaida Perić[13], Antonio M. Risitano[14], Annalisa Ruggeri[7], Isabel Sánchez-Ortega[15], John A. Snowden[16] and Anna Sureda[17]

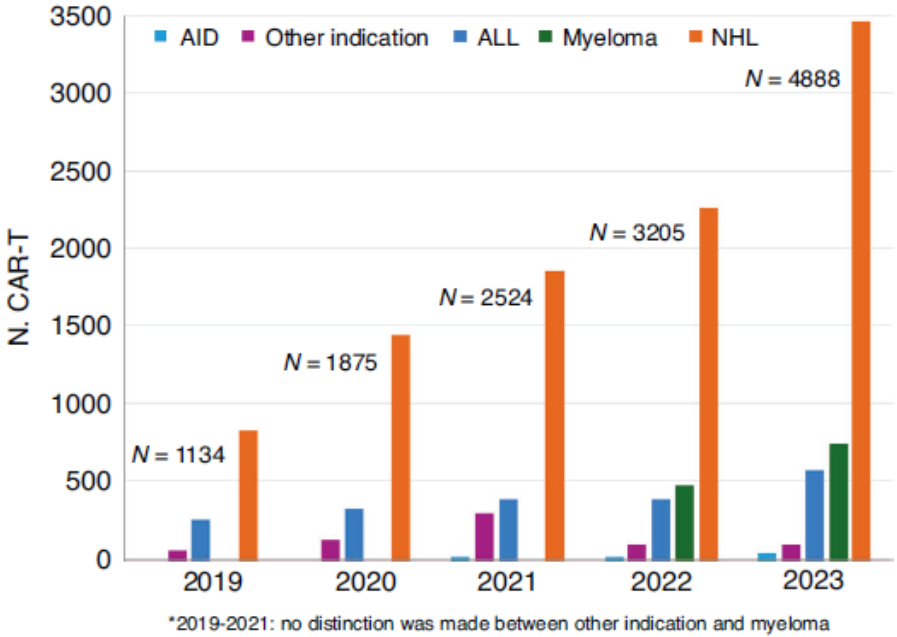


Fig. 5 Increase in the number of patients receiving CAR-T therapy by main indication from 2019 to 2023.

Comment le champ thérapeutique des immunothérapies cellulaires va-t-il évoluer?

- La progression de l'activité CAR-T cells est aujourd'hui impactée par l'irruption de nouvelles immunothérapies dans le champ des hémopathies lymphoïdes malignes
- Nouvelles indications ?
- Ruptures technologiques ?

The NEW ENGLAND JOURNAL of MEDICINE

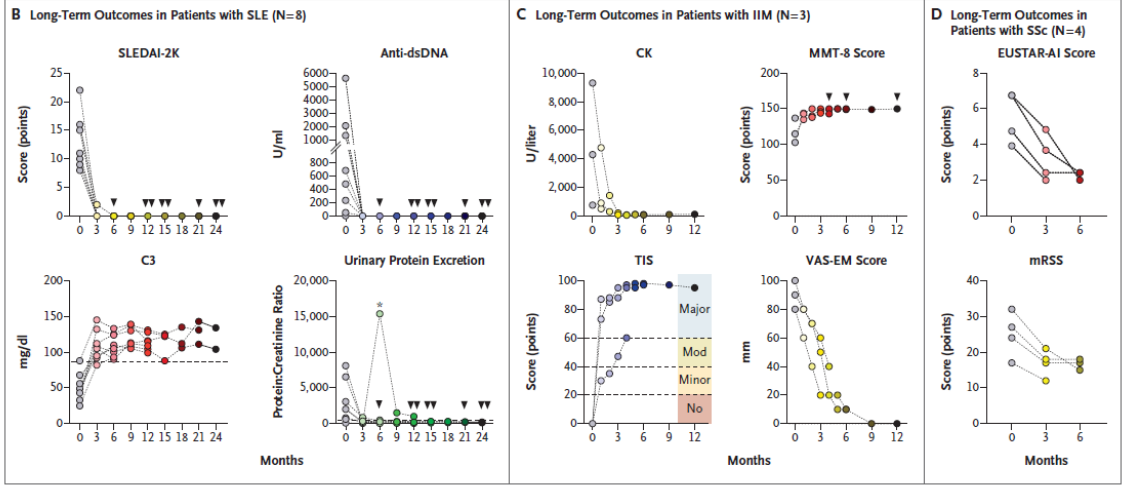
ESTABLISHED IN 1812 FEBRUARY 22, 2024 VOL. 390 NO. 8

CD19 CAR T-Cell Therapy in Autoimmune Disease — A Case Series with Follow-up

Fabian Müller, M.D., Jule Taubmann, M.D., Laura Bucci, M.D., Artur Wilhelm, Ph.D., Christina Bergmann, M.D., Simon Völkl, Ph.D., Michael Aigner, Ph.D., Tobias Rothe, Ph.D., Ioanna Minopoulou, M.D., Carlo Tur, M.D., Johannes Knitza, M.D., Soraya Kharboutli, M.D., Sascha Kretschmann, Ph.D., Ingrid Vasova, M.D., Silvia Spoerl, M.D., Hannah Reimann, Ph.D., Luis Munoz, M.D., Roman G. Gerlach, Ph.D., Simon Schäfer, Ph.D., Ricardo Grieshaber-Bouyer, M.D., Anne-Sophie Korganow, M.D., Dominique Farge-Bancel, M.D., Dimitrios Mougiakakos, M.D., Aline Bozec, Ph.D., Thomas Winkler, Ph.D., Gerhard Krönke, M.D., Andreas Mackensen, M.D., and Georg Schett, M.D.

A Short-Term Efficacy of CD19 CAR T-Cell Therapy in Autoimmune Disease

Patient No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Disease	SLE								IIM			SSc			
DORIS Remission	+	+	+	+	+	+	+	+*							
LLDAS	+	+	+	+	+	+	+	+*	N/A						
SLEDAI-2K Score	0	0	0	0	0	0	0	0				N/A			
ACR–EULAR Major Clinical Response									+	+	+*				
Normalization of CK Level	N/A								+	+	+*				
Change in EUSTAR-AI Score												−2.3	−4.7	−4.3	−1.9*
Change in mRSS									N/A			−7	−9	−17	−5*
Glucocorticoid-free State	+	+	+	+	+	+	+	+*	+	+	+*	+	+	+	+*
No Immunosuppressive Drugs	+	+	+	+	+	+	+	+*	+	+	+*	+	+	+	+*



Received: 29 November 2022 | Revised: 25 January 2023 | Accepted: 27 January 2023
DOI: 10.1002/jca.22043

Journal of Clinical Apheresis ... ASFA WILEY

Guidelines on the Use of Therapeutic Apheresis in Clinical Practice – Evidence-Based Approach from the Writing Committee of the American Society for Apheresis: The Ninth Special Issue

Laura Connelly-Smith[1] | Caroline R. Alquist[2] | Nicole A. Aqui[3] | Jan C. Hofmann[4] | Reinhard Klingel[5,6] | Oluwatoyosi A. Onwuemene[7] | Christopher J. Patriquin[8] | Huy P. Pham[9] | Amber P. Sanchez[10] | Jennifer Schneiderman[11] | Volker Witt[12] | Nicole D. Zantek[13] | Nancy M. Dunbar[14]

Sickle cell disease, acute	Acute stroke	RBC exchange	I	1C	215
	Acute chest syndrome, severe	RBC exchange	II	1C	
	Other complications[a]	RBC exchange/TPE	III	2C	
Sickle cell disease, non-acute	Stroke prophylaxis	RBC exchange	I	1A	217
	Pregnancy	RBC exchange	II	2B	
	Recurrent vaso-occlusive crises	RBC exchange	II	2B	
	Pre-operative management	RBC exchange	III	2A	
Steroid-responsive encephalopathy associated with autoimmune thyroiditis		TPE	II	2C	219
Stiff-person syndrome		TPE	III	2C	221
Sudden sensorineural hearing loss		LA/DFPP/TPE	III	2A	223
Systemic lupus erythematosus	Severe	TPE	II	2C	225
Systemic sclerosis		ECP	III	2A	227

CAR T day
9th International Symposium on Car T Cells
11-12 SEPTEMBER 2025
Faculté de médecine de Lille

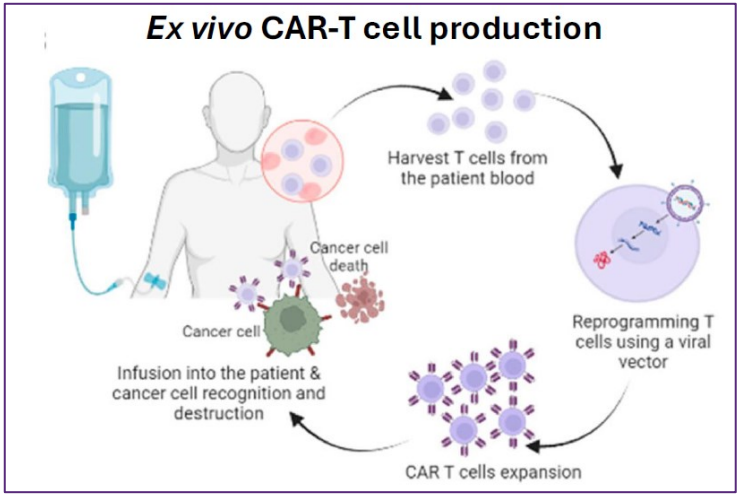
UNITC
consortium national de recherche sur les thérapies cellulaires et géniques

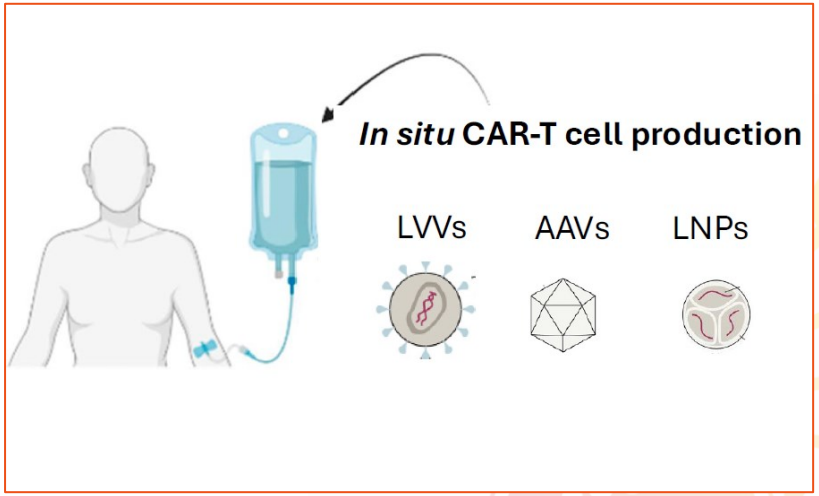
in vivo CAR Task force

Carole-Anne Brugère, PharmD
Institut Carnot Calym, UNITC

DESCAR-T
INSTITUT CARNOT CALYM
INSTITUT CARNOT OPALE
FITC
Société Française d'Immunologie
SFGM-TC Société Francophone de GREFFE DE MOELLE et de Thérapie Cellulaire

in vivo CAR T-cells?





Industrial *in vivo* CAR-T: a fast-moving field in 2025

July 24
1st *Investigational New Drug* (IND) approved by the FDA *(Interius, Umoja)*

Oct 24
1st patient included in a FIH trial (Interius)

Jan 25
4 heme candidates in phase I FIH
interius Umoja EsoBiotec

1st clinical trials FIH authorized in Europe
Interius Germany then Spain in B cell lymphoma

Mar 25
1B$
EsoBiotec
AstraZeneca

Apr 25
Ph I FIH in Australia in healthy volunteers

June 25
2,1B$
capstan therapeutics
abbvie

July 25
Data published on first 4 patients in the Lancet (Esobiotec)

Aug 25
350M$
interius
GILEAD

Au total

- Des pratiques évolutives et qui se diversifient :
  - Les Unités d'Aphérèse travaillent pour un nombre croissant de prescripteurs et de donneurs d'ordre
  - Doivent faire face à une plus grande diversité d'exigences en fonction de l'usage prévu pour les cellules prélevées
  - Les interactions avec les industriels de la pharmacie se traduisent par des exigences plus importantes

Comment faire face aux exigences et contraintes actuelles et futures ?

- Infrastructures
- Equipements
- Personnels

Adapter les infrastructures aux besoins quantitativement et qualitativement croissants

- Modèle centralisé vs multiplication des infrastructures ?
- Centralisation géographique vs centralisation basée sur les usages ?
- Service rendu aux patients ET soutenabilité économique

Adapter les équipements aux besoins quantitativement et qualitativement croissants

- Nombre de séparateurs disponibles
- Amélioration des performances des séparateurs ?
  - Permettant un monitorage et un pilotage plus précis et en temps réel du prélèvement ?

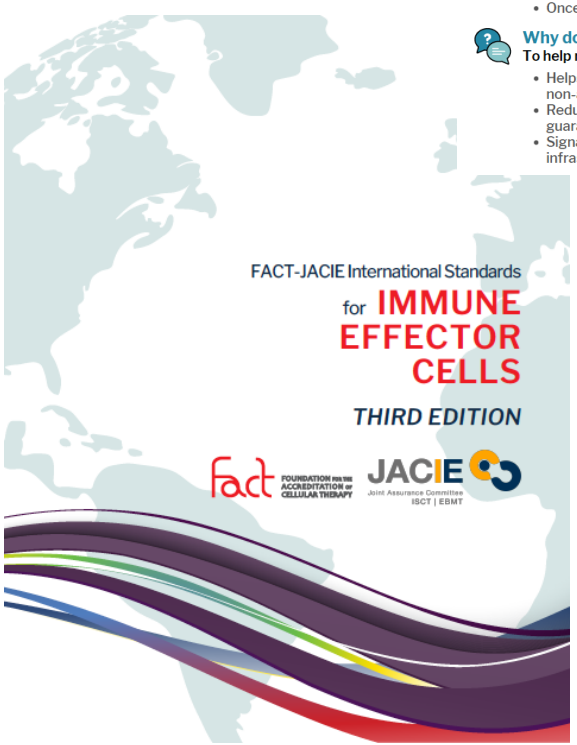
Former et fidéliser les personnels

- Personnels infirmiers
- Personnels médicaux
  - Formation initiale : médecins généralistes, médecins spécialistes ?
    - Apprentissage de certaines tâches ou conduites à tenir spécifiques à certaines thérapies cellulaires ou géniques

~~- Possibilité de délégation de tâches à des IPA ?~~

« Qualification » des centres

- Par les tutelles sanitaires
- Par les laboratoires pharmaceutiques détenteurs des AMM
  - Multiplication des évaluations / audits
  - FACT / JACIE Standards



FAQ: FACT Provisional Clinical Accreditation

ABOUT PROVISIONAL ACCREDITATION

What is FACT's provisional clinical accreditation?

A pathway for new cellular therapy programs that haven't yet treated the minimum number of patients for full accreditation.

- Demonstrates compliance with all FACT Standards except for those regarding patient volume and provider experience.
- Intended to increase access to safe, high-quality cellular therapies closer to where patients live and work.
- Once minimum patient numbers are met, programs can pursue full accreditation.

Why does FACT offer provisional accreditation?

To help new programs safely provide cellular therapies while addressing real-world barriers.

- Helps programs overcome the "minimum patient conundrum," especially in community or non-academic settings.
- Reduces financial risk related to treating the minimum patient numbers without guaranteed reimbursement.
- Signals to payers and stakeholders that the program has the necessary training, infrastructure, and quality systems.

Conclusion (1)

- L’expérience acquise depuis deux décennies montre que l’accès aux thérapies cellulaires et géniques ne passe pas uniquement par l’élucidation de mécanismes physiopathologiques et l’identification de mécanismes activables
- La mise en place de circuits thérapeutiques complexes et couteux est un obstacle supplémentaire au prix élevé de ces médicaments

Conclusion (2)

- Pour les thérapies cellulaires les plus prescrites / utilisées, fabriquées à partir de cellules hématopoïétiques humaines, la collecte initiale des cellules sanguines par cytaphérèse est une étape critique du procédé de fabrication
- L'adaptation des moyens est et sera nécessaire, mais l'ampleur des adaptations volumétriques et la définition des organisations optimales nécessite de poursuivre collectivement cette réflexion

Remerciements

- Institut Paoli-Calmettes
  - Centre de Thérapie Cellulaire
    - Unité de Cytaphérèse:
      - Dr Angéla Granata
      - ***Christelle Andorno***
      - ***Marie-Pierre d'Ingrando†***
      - ***Aurélie Festa***
      - ***Jérôme Georgeton***
      - ***Mickael Guichot***
      - ***Gaelle Heude***
      - Caroline Golfetto
      - Farida Braham
    - Unité de Thérapie Cellulaire
  - Département de Biologie du Cancer
  - Département d'Oncohématologie
  - Département d'Oncologie médicale
- AP-HM & AMU
  - Département d'Hématologie, Immunologie et Oncologie pédiatriques. Hopital Timone-Enfants
  - Laboratoire de Culture et de Thérapie Cellulaire (LCTC). Hôpital de la Conception
  - Module Biothérapies du Centre d'Investigations Cliniques de Marseille, CBT-1409
  - UMR 7318 Droits International, Comparé et européen (DICE)
- EBMT / EHA / GoCART Coalition / JACIE