Actualités 2019

Marie Thérèse Rubio
CS de la SFGM-TC

Nantes, 6 Novembre 2019

Les grands axes

- **Conditionnement RIC:** Fluda-Treosulfan fait mieux que Fluda-Busulfan
- **GVH:**
  - En prophylaxie: PT-Cy or ATG ?
  - En curatif Ruxolitinib: FDA approved !
- **Infections: ECIL7 :** Letermovir en prophylaxie du CMV
- **Mécanismes d'échappement immunitaire post-allogreffe**
- **CAR-T cells**:
  - Résultats dans le myélome
  - Mécanismes d'échappement et dual/multi-CAR
  - CAR-T et inhibiteurs de check point
  - Dasatinib en prévention du CRS
  - CAR-T bridge vers l'allogreffe : chez qui ?

- **Gilteritinib dans la LAM R/R :** avant et après la greffe

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Treosulfan or busulfan plus fludarabine as conditioning treatment before allogeneic haemopoietic stem cell transplantation for older patients with acute myeloid leukaemia or myelodysplastic syndrome (MC-FludT.14/L): a randomised, non-inferiority, phase 3 trial

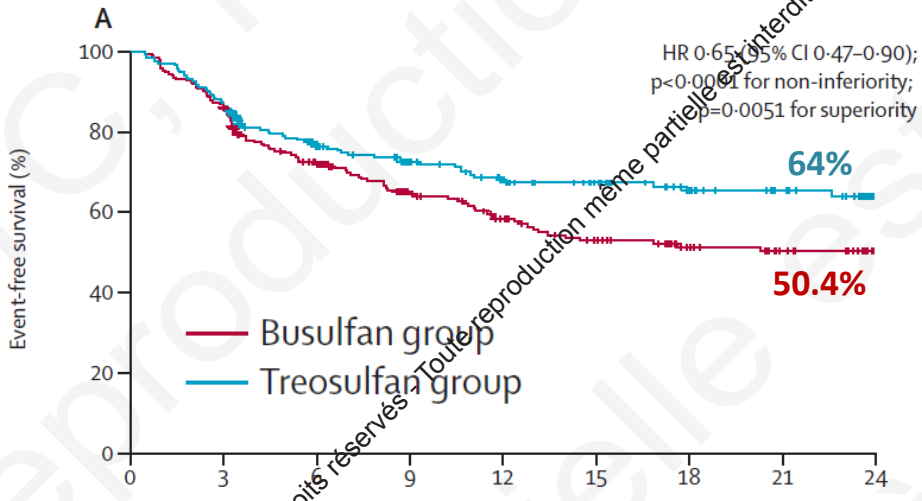
Dietrich Wilhelm Beelen, Rudolf Trenschel, Matthias Stelljes, Christoph Groth, Tamás Masszi, Péter Reményi, Eva-Maria Wagner-Drouet, Beate Hauptrock, Peter Dreger, Thomas Luft, Wolfgang Bethge, Wichard Vogel, Fabio Ciceri, Jacopo Peccatori, Friedrich Stölzel, Johannes Schetelig, Christian Junghanß, Christina Grosse-Thie, Mauricette Michallet, Hélène Labussiere-Wallet, Kerstin Schaefer-Eckart, Sabine Dressler, Goetz Ulrich Grigoleit, Stephan Mielke, Christof Scheid, Udo Holtick, Francesca Patriarca, Marta Medeot, Alessandro Rambaldi, Maria Caterina Micò, Dietger Niederwieser, Georg-Nikolaus Franke, Inken Hilgendorf, Nils Rudolf Winkelmann, Domenico Russo, Gérard Socié, Régis Peffault de Latour, Ernst Holler, Daniel Wolff, Bertram Glass, Jochen Casper, Gerald Wulf, Helge Menzel, Nadezda Basara, Maria Bieniaszewska, Gernot Stuhler, Mareike Verbeek, Sandra Grass, Anna Paola Iori, Juergen Finke, Fabio Benedetti, Uwe Pichlmeier, Claudia Hemmelmann, Michael Tribanek, Anja Klein, Heidrun Anke Mylius, Joachim Baumgart, Monika Dzierzak-Mietla, Mirosław Markiewicz

Lancet Haematol 2019

Published online October 9, 2019 https://doi.org/10.1016/S2352-3026(19)30157-7

	Busulfan plus fludarabine group (n=240)	Treosulfan plus fludarabine group (n=220)
All patients		
Age, years		
Median	61·0 (56·5–64·0)	60·0 (55·0–65·0)
≥50	229/240 (95%)	205/220 (93%)
Comorbidity		
HCT-CI score	3·0 (1·0–4·0)	3·0 (1·0–4·0)
HCT-CI score >2	140/240 (58%)	131/220 (60%)
Donor type		
Matched related donor	59/240 (25%)	52/220 (24%)
Matched unrelated donor	181/240 (75%)	168/220 (76%)
Graft source		
Peripheral blood	235/240 (98%)	214/220 (97%)
Bone marrow	5/240 (2%)	6/220 (3%)
Diagnosis		
Acute myeloid leukaemia	138/240 (58%)	155/220 (71%)
Myelodysplastic syndrome	102/240 (43%)	65/220 (30%)
AML		
Risk group*		
Low risk	13/138 (9%)	15/155 (10%)
Intermediate risk	61/138 (44%)	55/155 (36%)
High risk	43/138 (31%)	63/155 (41%)
Not applicable (if > complete remission 1)	21/138 (15%)	22/155 (14%)
MDS		
Risk group based on IPSS-R		
Very low risk	1/102 (1%)	5/65 (8%)
Low risk	16/102 (16%)	13/65 (20%)
Intermediate risk	30/102 (29%)	11/65 (17%)
High risk	24/102 (24%)	16/65 (25%)
Very high risk	31/102 (30%)	20/65 (31%)

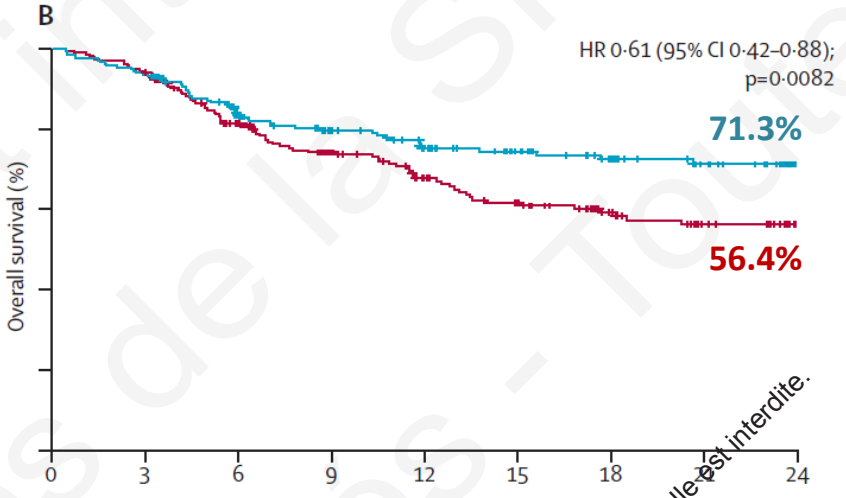
EFS



Number at risk (number censored)

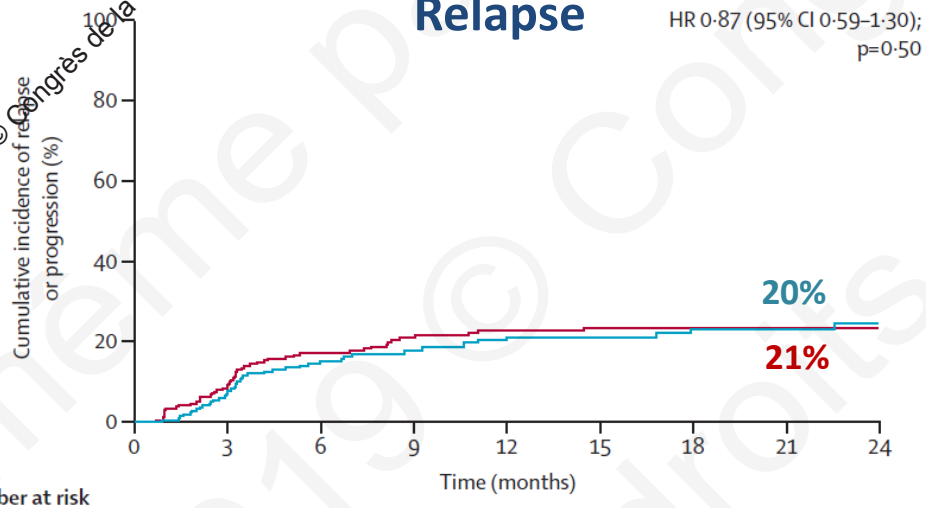
Busulfan group	240 (0)	206 (3)	151 (25)	112 (50)	92 (59)	74 (69)	57 (84)	44 (96)	25 (117)
Treosulfan group	220 (0)	190 (0)	144 (27)	121 (45)	97 (59)	82 (73)	62 (91)	49 (104)	16 (138)

OS



	240 (0)	227 (2)	172 (27)	133 (52)	107 (66)	87 (77)	65 (96)	48 (110)	27 (133)
	220 (0)	206 (0)	159 (28)	133 (50)	107 (65)	88 (83)	68 (101)	54 (114)	18 (152)

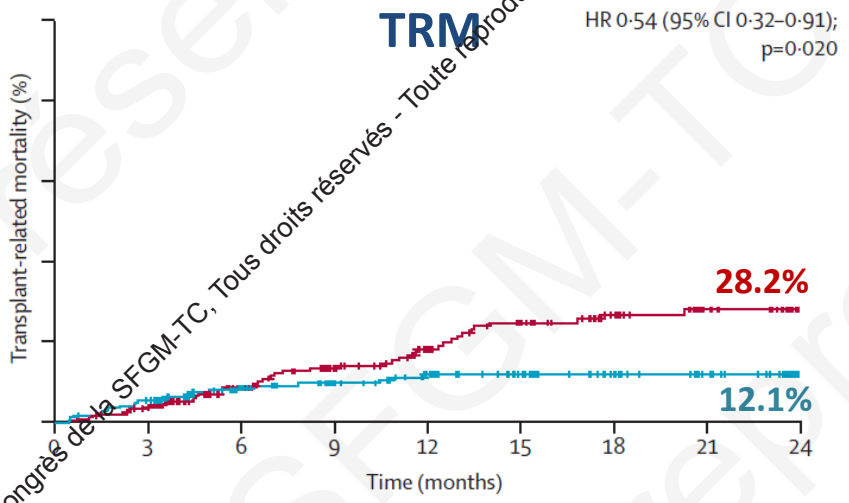
Relapse



Number at risk (number censored)

Busulfan group	240 (0)	206 (3)	151 (25)	112 (50)	92 (59)	74 (69)	57 (84)	44 (96)	25 (117)
Treosulfan group	220 (0)	190 (0)	144 (27)	121 (45)	97 (59)	82 (73)	62 (91)	49 (104)	16 (138)

TRM



	240 (0)	227 (7)	172 (50)	133 (81)	107 (99)	87 (111)	65 (131)	48 (147)	27 (170)
	220 (0)	206 (2)	159 (44)	133 (71)	107 (90)	88 (109)	68 (129)	54 (143)	18 (181)

	Busulfan plus fludarabine group (n=240)	Treosulfan plus fludarabine group (n=220)	HR (95% CI)	p value
Transplantation-related mortality				
Patients with event¶	45 (19%)	23 (10%)	..	..
GvHD	18 (8%)	10 (5%)	..	..
Haemorrhage	1 (<1%)	1 (<1%)	..	..
Renal failure	0	5 (2%)	..	..
Cardiac toxicity	4 (2%)	1 (<1%)	..	..
Interstitial pneumonitis	0	1 (<1%)	..	..
Central nervous system toxicity	1 (<1%)	0	..	..
Veno-occlusive disease or hepatic sinusoidal obstruction syndrome	1 (<1%)	0	..	..
Infection	30 (13%)	19 (9%)	..	..
Multiple organ failure	5 (2%)	5 (2%)	..	..
Other transplantation-related cause	1 (<1%)	0	..	..
Patients with event later than 6 months after transplantation¶	26 (11%)	5 (2%)	..	..
GvHD	7 (3%)	3 (1%)	..	..
Renal failure	0	1 (<1%)	..	..
Cardiac toxicity	4 (2%)	1 (<1%)	..	..
Central nervous system toxicity	1 (<1%)	0	..	..
Infection	17 (7%)	3 (1%)	..	..
Multiple organ failure	2 (1%)	1 (<1%)	..	..
24-month transplantation-related mortality (95% CI)	28·2% (21·4–36·5)	12·1% (8·1–17·7)	0·54 (0·32–0·91)	0·020‡

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Three prophylaxis regimens (tacrolimus, mycophenolate mofetil, and cyclophosphamide; tacrolimus, methotrexate, and bortezomib; or tacrolimus, methotrexate, and maraviroc) versus tacrolimus and methotrexate for prevention of graft-versus-host disease with haemopoietic cell transplantation with reduced-intensity conditioning: a randomised phase 2 trial with a non-randomised contemporaneous control group (BMT CTN 1203)

Javier Bolaños-Meade, Ran Reshef*, Raphael Fraser, Mingwei Fei, Sunil Abhyankar, Zaid Al-Kadhimi, Amin M Alousi, Joseph H Antin, Sally Arai, Kate Bickett, Yi-Bin Chen, Lloyd E Damon, Yvonne A Efebera, Nancy L Geller, Sergio A Giralt, Parameswaran Hari, Shernan G Holtan, Mary M Horowitz, David A Jacobsohn, Richard J Jones, Jane L Liesveld, Brent R Logan, Margaret L MacMillan, Marco Mielcarek, Pierre Noel, Joseph Pidala, David L Porter, Iskra Pusic, Ronald Sobecks, Scott R Solomon, Daniel J Weisdorf, Juan Wu, Marcelo C Pasquini†, John Koreth†*

Lancet Haematol 2019;
6: e132–43

Vol 6 March 2019

31 US centers
Different conditionings allowed
PBSC graft

Sibling donors or 8/8 or 7/8 HLA MUD
Any hematological disease

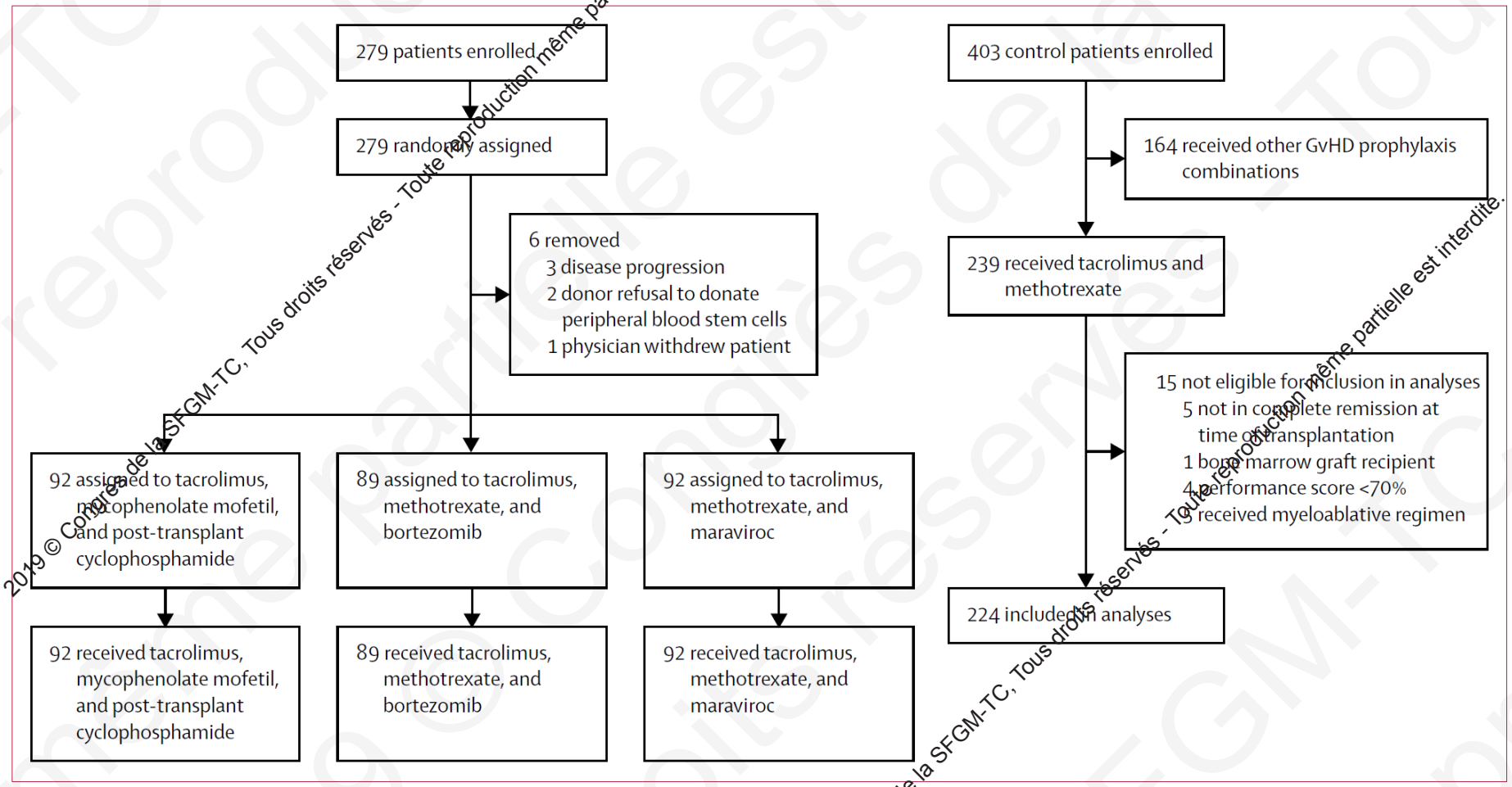
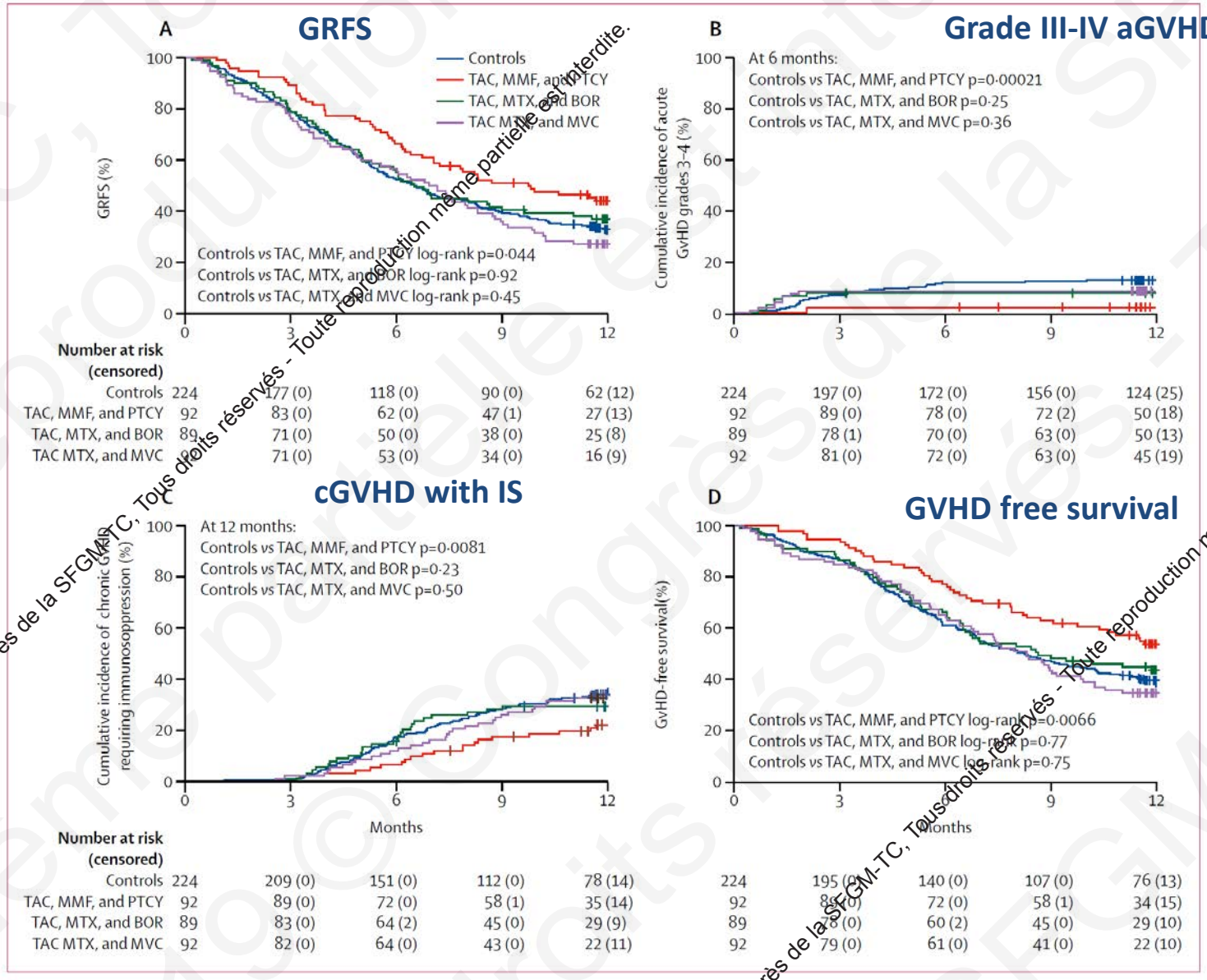


Figure 1: **Trial profile**
GvHD=graft-versus-host disease.

Bortezomib &.3 mg/m2 on D1, D4 and D7 post-HSCT
Maraviroc= anti-CCR5 (homing of T cells to GI) D-3 to D+30



Interpretation Tacrolimus, mycophenolate mofetil, and post-transplantation cyclophosphamide was the most promising intervention, yielding the best GRFS; this regimen is thus being prospectively compared with tacrolimus and methotrexate in a phase 3 randomised trial.

Acute GVHD prophylaxis plus ATLG after myeloablative allogeneic haemopoietic peripheral blood stem-cell transplantation from HLA-identical siblings in patients with acute myeloid leukaemia in remission: final results of quality of life and long-term outcome analysis of a phase 3 randomised study

Francesca Bonifazi, Carlos Solano, Christine Wolschke, Mariarosaria Sessa, Francesca Patriarca, Francesco Zallio, Arnon Nagler, Carmine Selleri, Antonio Maria Risitano, Giuseppe Messina, Wolfgang Bethge, Pilar Herrera, Anna Sureda, Angelo Michele Carella, Michele Cimminiello, Stefano Gabbi, Jürgen Finke, Roberto Sorasio, Christelle Ferra, Jorge Sierra, Domenico Russo, Edoardo Benedetti, Giuseppe Milone, Fabio Benedetti, Marion Heinzelmann, Domenico Pastore, Manuel Jurado, Elisabetta Terruzzi, Franco Narni, Andreas Völp, Francis Ayuk, Tapani Ruutu, Nicolaus Kröger

Lancet Haematol 2019;
6: e89–99

Vol 6 February 2019

MAC : FB4 ATG-G 30 mg/kg
Sibling PBSC

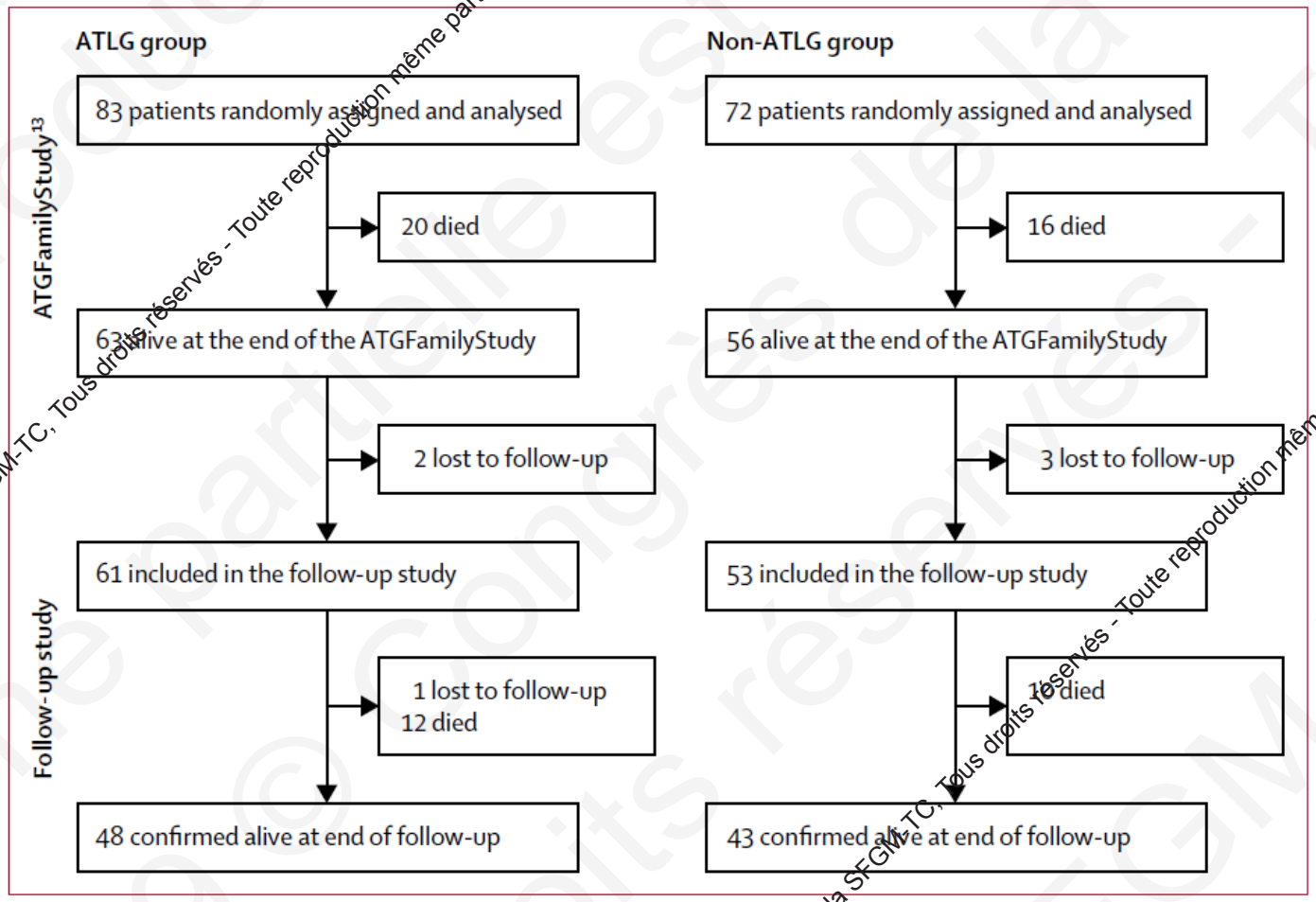
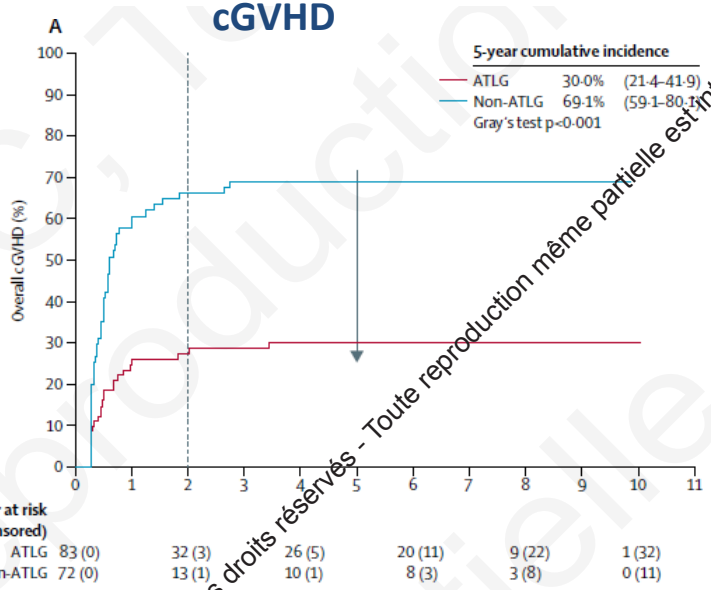
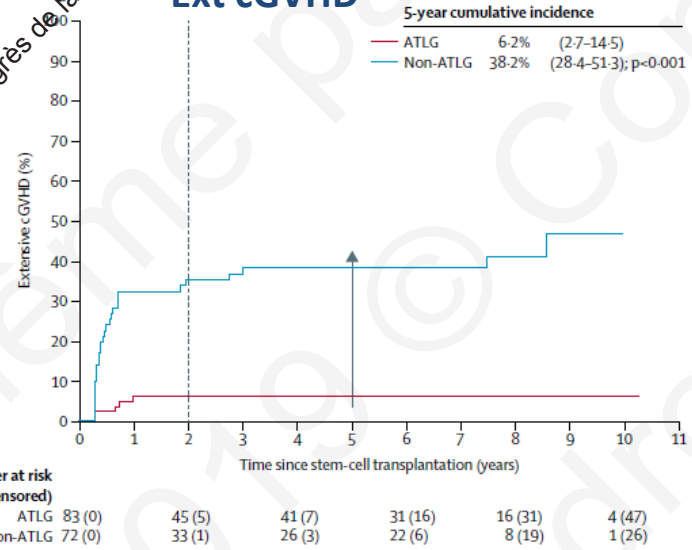


Figure 1: **Trial profile**
ATLG=anti-T-lymphocyte globulin.

cGVHD



Ext cGVHD



Quality of life

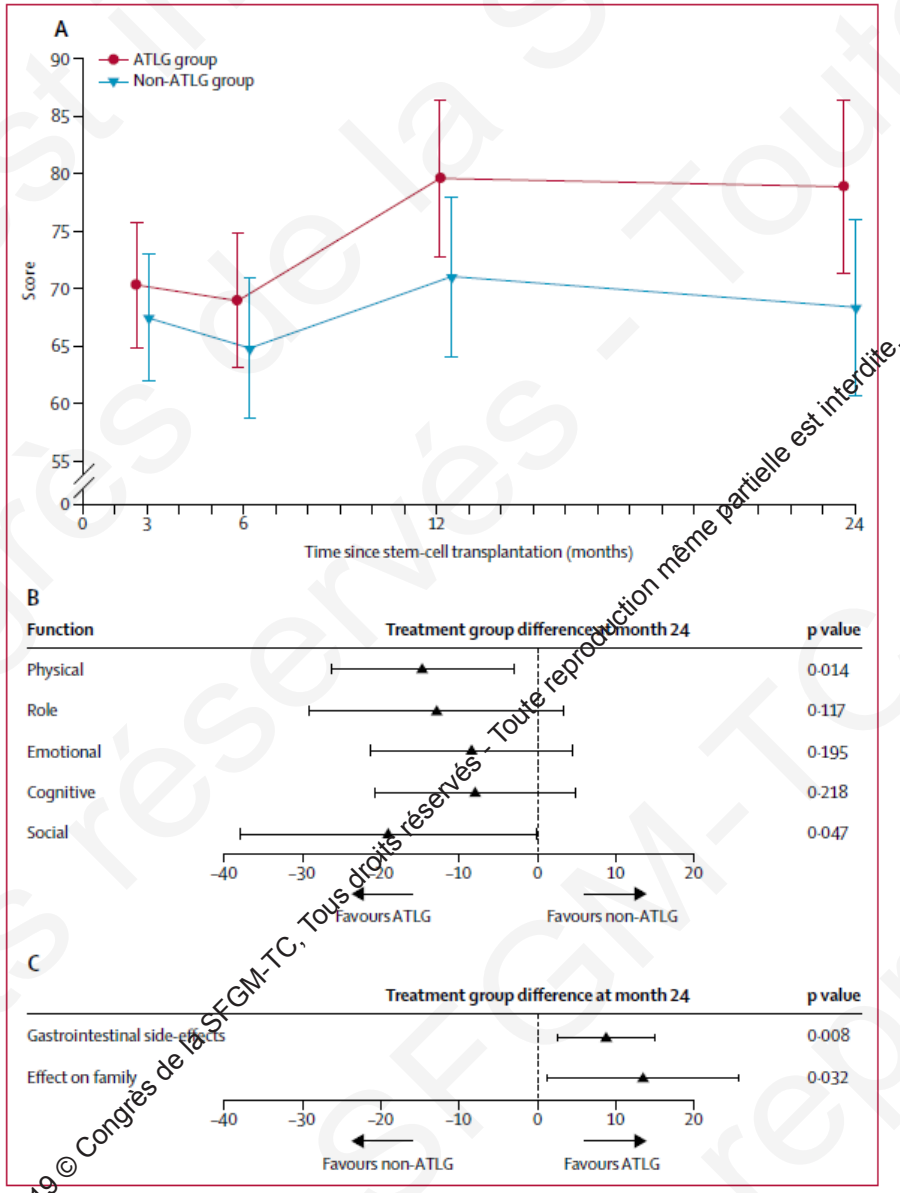
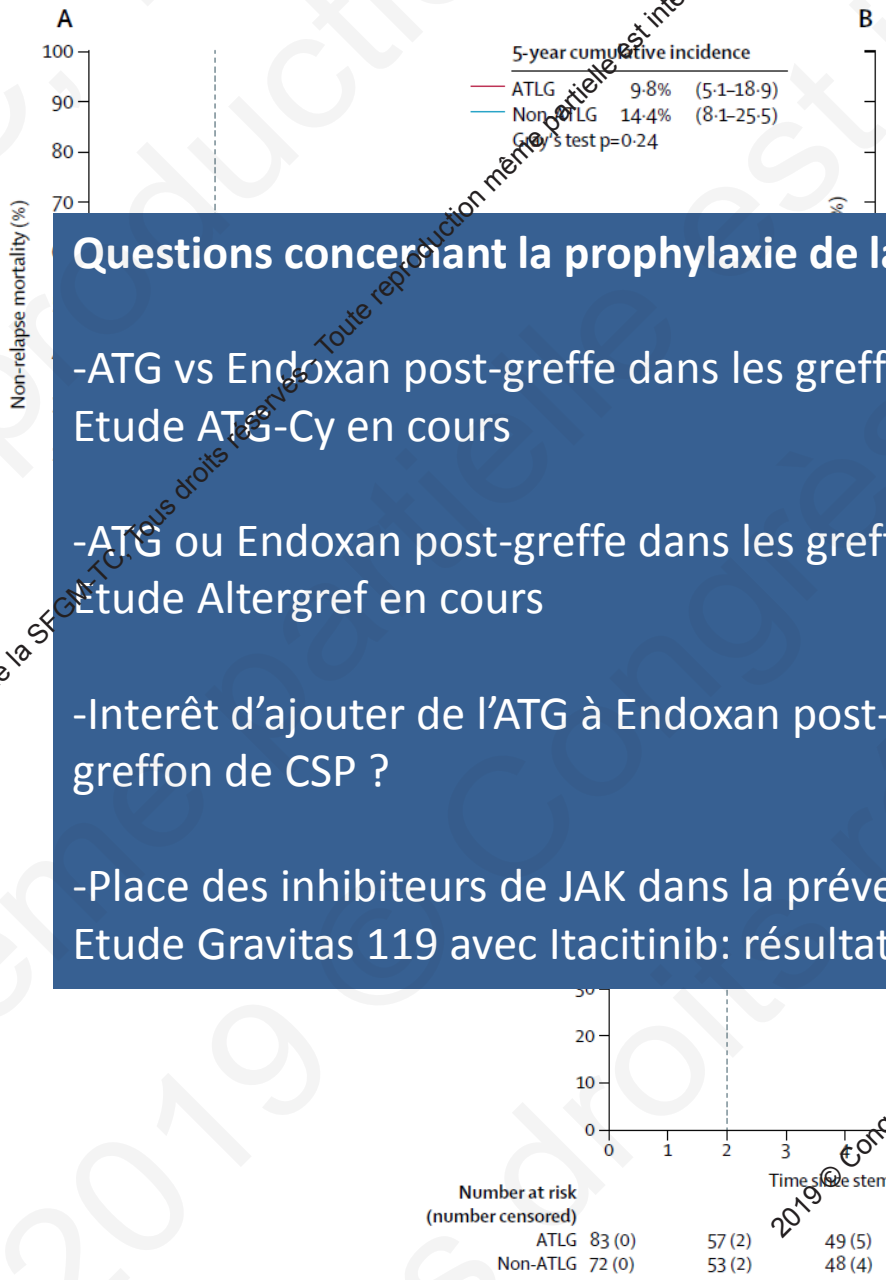


Figure 2: Quality-of-life analysis

NRM

Relapse incidence



Questions concernant la prophylaxie de la GVH:

-ATG vs Endoxan post-greffe dans les greffes avec donneur phénoidentique ? : Etude ATG-Cy en cours

-ATG ou Endoxan post-greffe dans les greffes phéno 9/10 ?
Etude Altergref en cours

-Interêt d'ajouter de l'ATG à Endoxan post-greffe en haploidentique avec greffon de CSP ?

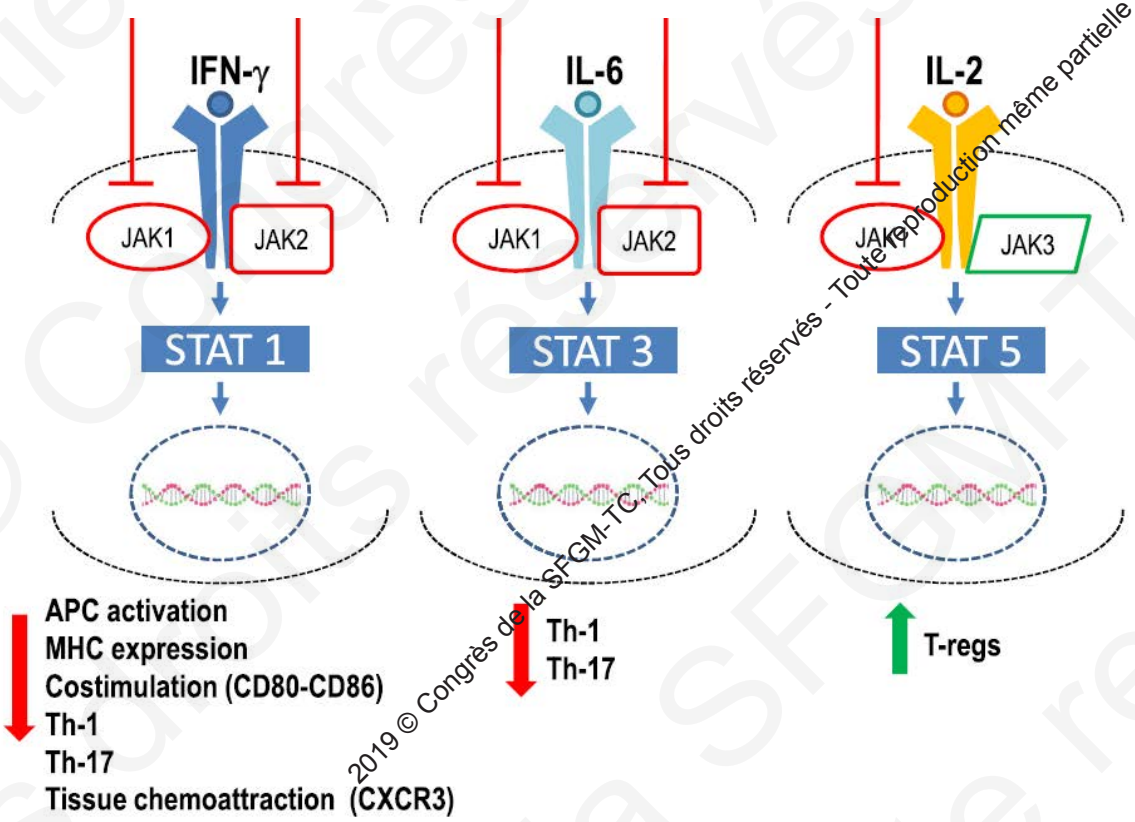
-Place des inhibiteurs de JAK dans la prévention de la GVH ?
Etude Gravitas 119 avec Itacitinib: résultats en attente

Drugs
https://doi.org/10.1007/s40265-019-01174-1

LEADING ARTICLE

Janus Kinase Inhibition for Graft-Versus-Host Disease: Current Status and Future Prospects

Daniele Mannina[1,2] · Nicolaus Kröger[1]



The Oncologist®

FDA Approval Summary: Ruxolitinib for Treatment of Steroid-Refractory Acute Graft-Versus-Host Disease

Donna Przepiorka,[a] Lola Luo,[a] Sriram Subramaniam,[a] Junshan Qiu,[a] Ramadevi Gudi,[a] Lea C. Cunningham,[a] Lei Nie,[a] Ruby Leong,[a] Lian Ma,[a] Christopher Sheth,[a] Albert Deisseroth,[a] Kirsten B. Goldberg,[b] Gideon M. Blumenthal,[b] Richard Pazdur[b]

[a]Center for Drug Evaluation and Research and [b]Oncology Center of Excellence, U.S. Food and Drug Administration, Silver Spring, Maryland, USA

Disclosures of potential conflicts of interest may be found at the end of this article.

Key Words. Ruxolitinib • Graft-versus-host disease • Hematopoietic stem cell transplantation

Abstract

On May 24, 2019, the Food and Drug Administration approved ruxolitinib for steroid-refractory acute graft-versus-host disease (SR-aGVHD) in adult and pediatric patients 12 years and older. Approval was based on Study INCB 18424-271 (REACH-1; NCT02953678), an open-label, single-arm, multicenter trial that included 49 patients with grades 2–4 SR-aGVHD occurring after allogeneic hematopoietic stem cell transplantation. Ruxolitinib was administered at 5 mg twice daily, with dose increases to 10 mg twice daily permitted after 3 days in the absence of toxicity. The Day-28 overall response rate was 57.1% (95% confidence interval [CI]: 42.2–71.2). The median duration of response was 0.5 months (95% CI: 0.3–3.7), and the median time from Day-28 response to either death or need for new therapy for acute GVHD was 5.7 months (95% CI: 2.2 to not estimable). Common adverse reactions included anemia, thrombocytopenia, neutropenia, infections, edema, bleeding, and elevated transaminases. Ruxolitinib is the first drug approved for treatment of SR-aGVHD. ***The Oncologist*** 2019;24:1–7

Implications for Practice: Ruxolitinib is the first Food and Drug Administration–approved treatment for steroid-refractory acute graft-versus-host disease in adult and pediatric patients 12 years and older. Its approval provides a treatment option for the 60% of those patients who do not respond to steroid therapy.

Guidelines for the management of cytomegalovirus infection in patients with haematological malignancies and after stem cell transplantation from the 2017 European Conference on Infections in Leukaemia (ECIL 7)

*Per Ljungman, Rafael de la Camara, Christine Robin, Roberto Crocchiolo, Hermann Einsele, Joshua A Hill, Petr Hubacek, David Navarro, Catherine Cordonnier, Katherine N Ward, on behalf of the 2017 European Conference on Infections in Leukaemia group**

Lancet Infect Dis 2019

Recommandations for antiviral prophylaxis after allogeneic HSCT

	European Society of Clinical Microbiology and Infectious Diseases recommendation grading[4]	Study	Comment
Aciclovir	CI	Prentice et al (1994)[92] Milano (2011)[93]	Less effective than valaciclovir
Valaciclovir	BI	Ljungman (2002)[94] Winston (2003)[95] Milano (2011)[93]	Used together with pre-emptive therapy
Ganciclovir	CI	Winston (1993)[96] Goodrich (1993)[97]	Used at engraftment
Valganciclovir	CIIh	Montesinos (2009)[98] Boeckh (2015)[99]	Cord blood HSCT used in Montesinos et al;[98] prophylaxis against late cytomegalovirus disease
Foscarnet	DIIu	Ordemann (2000)[100] Bregante (2000)[101]	NA
Letermovir	AI	Marty (2017)[7]	Only effective against cytomegalovirus

HSCT=haematopoietic stem cell transplantation. NA=not applicable.

Table: **Recommended drugs for antiviral prophylaxis after allogeneic HSCT**

WILEY

Transpl Infect Dis. 2019;00:e13187.
https://doi.org/10.1111/tid.13187

Letermovir for primary and secondary cytomegalovirus prevention in allogeneic hematopoietic cell transplant recipients: Real-world experience

Andrew Lin[1] | Molly Maloy[2] | Yiqi Su[3] | Valkal Bhatt[1] | Lauren DeRespiris[1] | Meagan Griffin[1] | Carmen Lau[1] | Anthony Proli[1] | Juliet Barker[2,4] | Brian Shaffer[2,4] | Sergio A. Giralt[2,4] | Ann A. Jakubowski[2,4] | Esperanza B. Papadopoulos[2,4] | Genovefa A. Papanicolaou[3,4] | Susan K. Seo[3,4] | Miguel-Angel Perales[2,4]

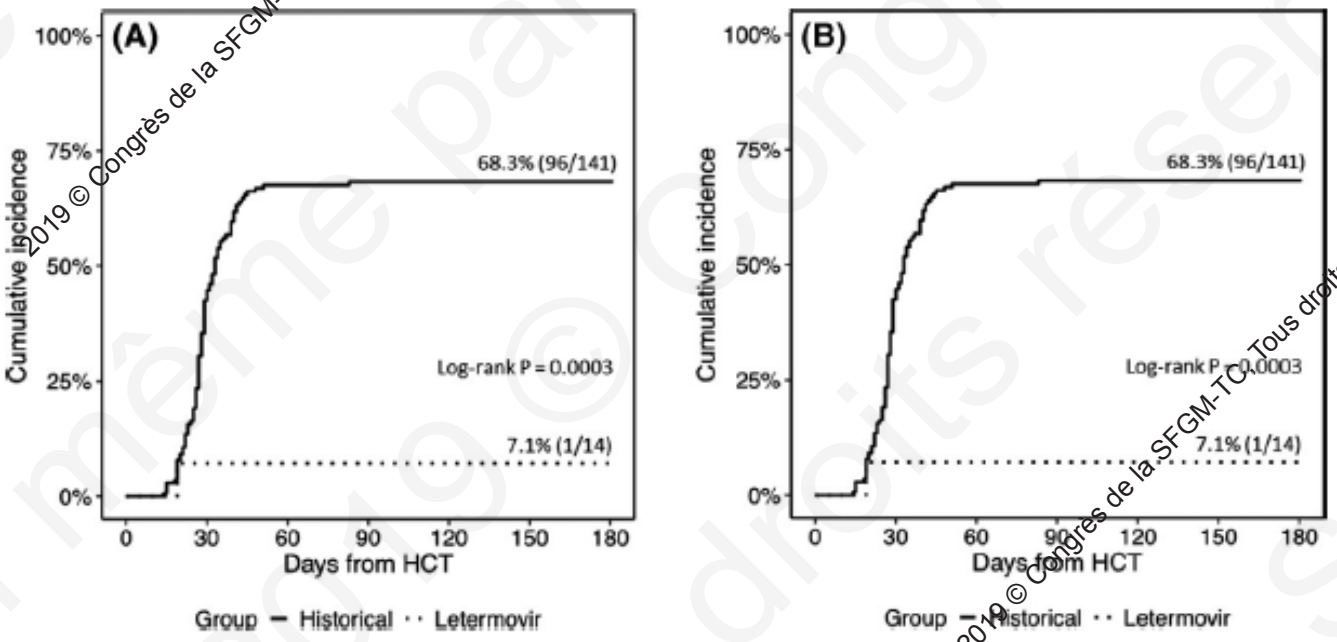


FIGURE 1 A, Cumulative incidence of CMV viremia by D + 180 in CMV R + TCD allo-HCT. B, Cumulative incidence of CMV end-organ disease by one year in CMV R + TCD allo-HCT

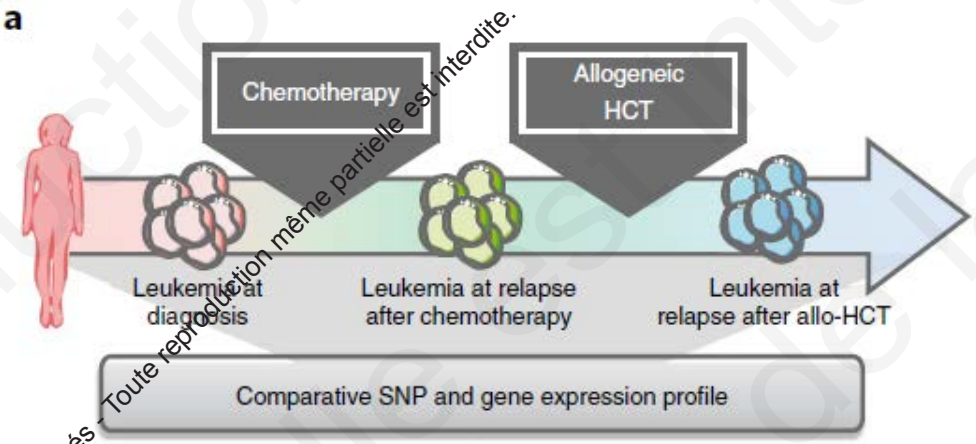
nature medicine

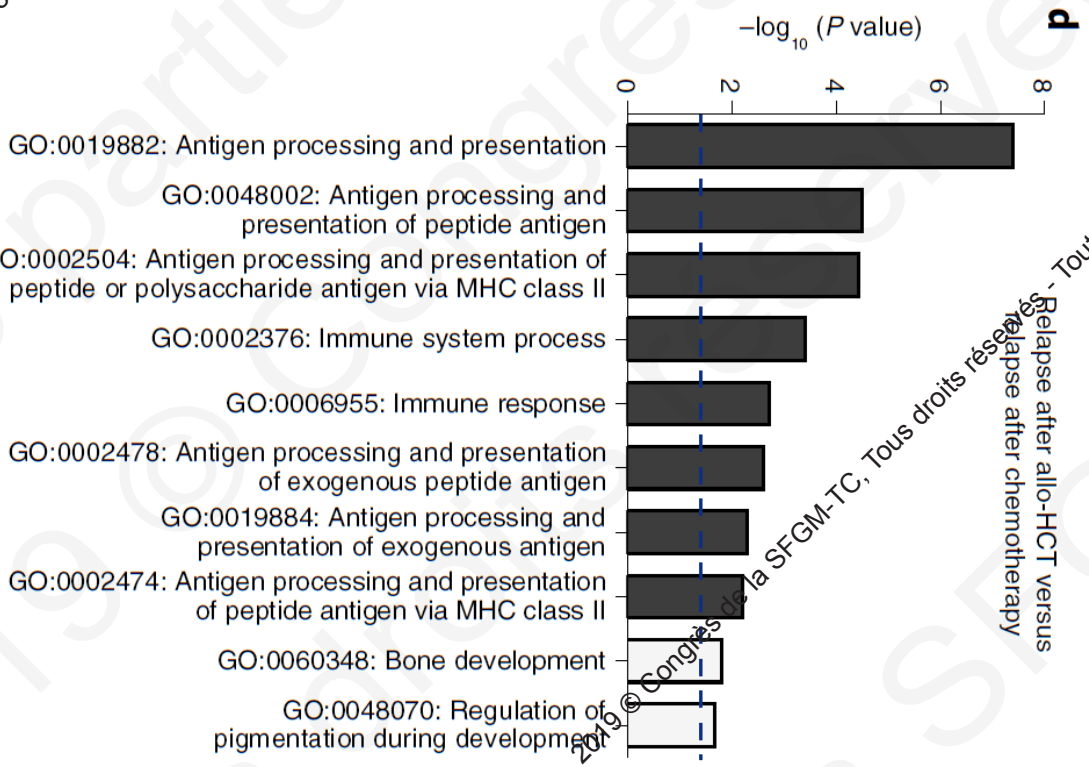
LETTERS

https://doi.org/10.1038/s41591-019-0400-z

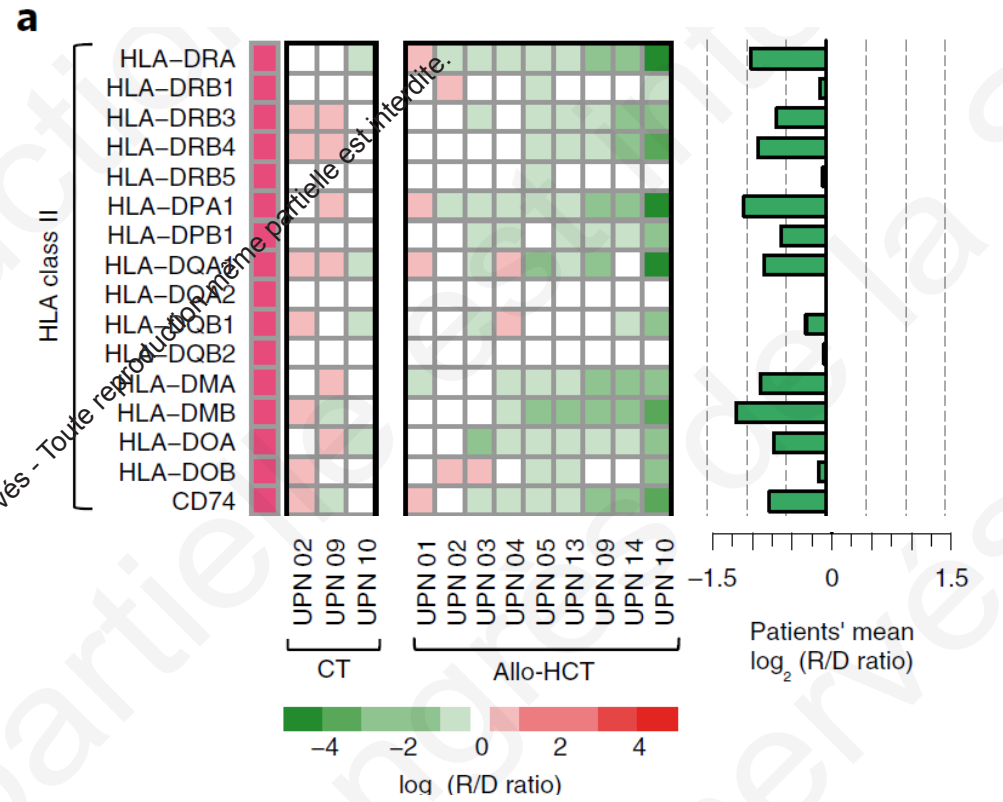
Immune signature drives leukemia escape and relapse after hematopoietic cell transplantation

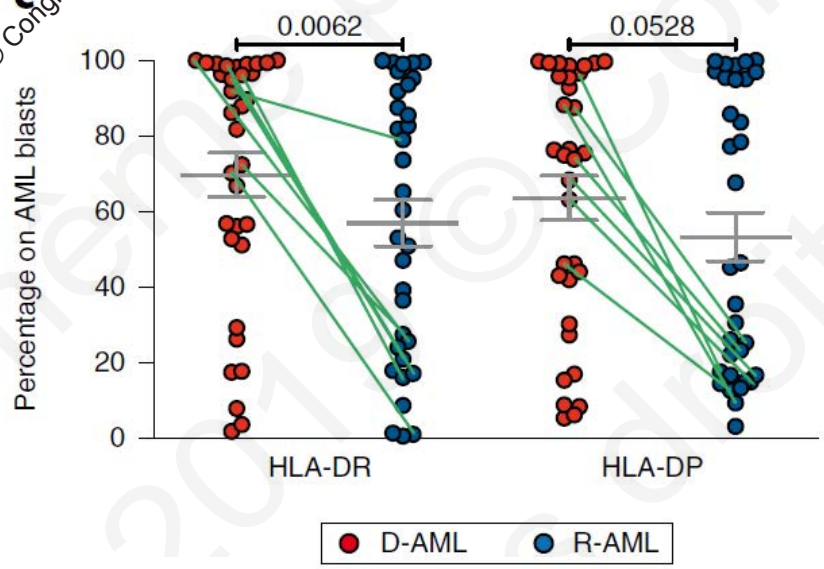
Cristina Toffalori[1,21], Laura Zito[1,21], Valentina Gambacorta[1,2,21], Michela Riba[3,21], Giacomo Oliveira[1,4,19], Gabriele Bucci[1,3], Matteo Barcella[5], Orietta Spinelli[6], Raffaella Greco[7], Lara Crucitti[7,20], Nicoletta Cieri[4,7,20], Maddalena Noviello[4], Francesco Manfredi[4], Elisa Montaldo[8], Renato Ostuni[8], Matteo M. Naldini[9], Bernhard Gentner[7,9], Miguel Waterhouse[10], Robert Zeiser[10], Jurgen Finke[10], Maher Hanoun[11], Dietrich W. Beelen[11], Ivana Gojo[12], Leo Luznik[12], Masahiro Onozawa[13], Takanori Teshima[13], Raynier Devillier[14], Didier Blaise[14], Constantijn J. M. Halkes[15], Marieke Griffioen[15], Matteo G. Carrabba[7], Massimo Bernardi[7], Jacopo Peccatori[7], Cristina Barlassina[5], Elia Stupka[3,19], Dejan Lazarevic[3], Giovanni Tonon[3], Alessandro Rambaldi[6,16], Davide Cittaro[3], Chiara Bonini[4,17], Katharina Fleischhauer[1,18], Fabio Ciceri[7,17,22] and Luca Vago[1,7,22]*

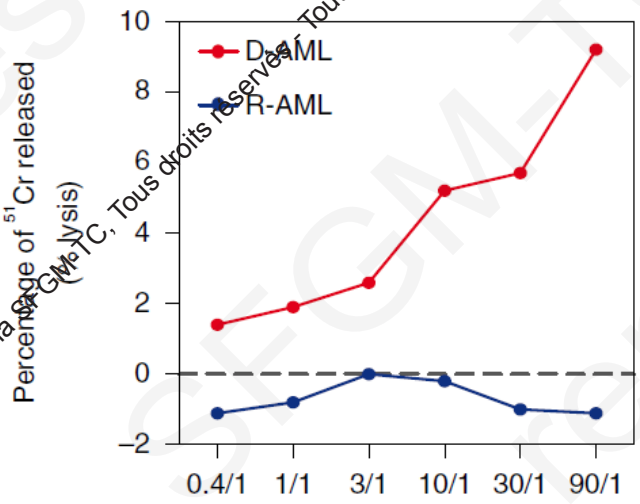




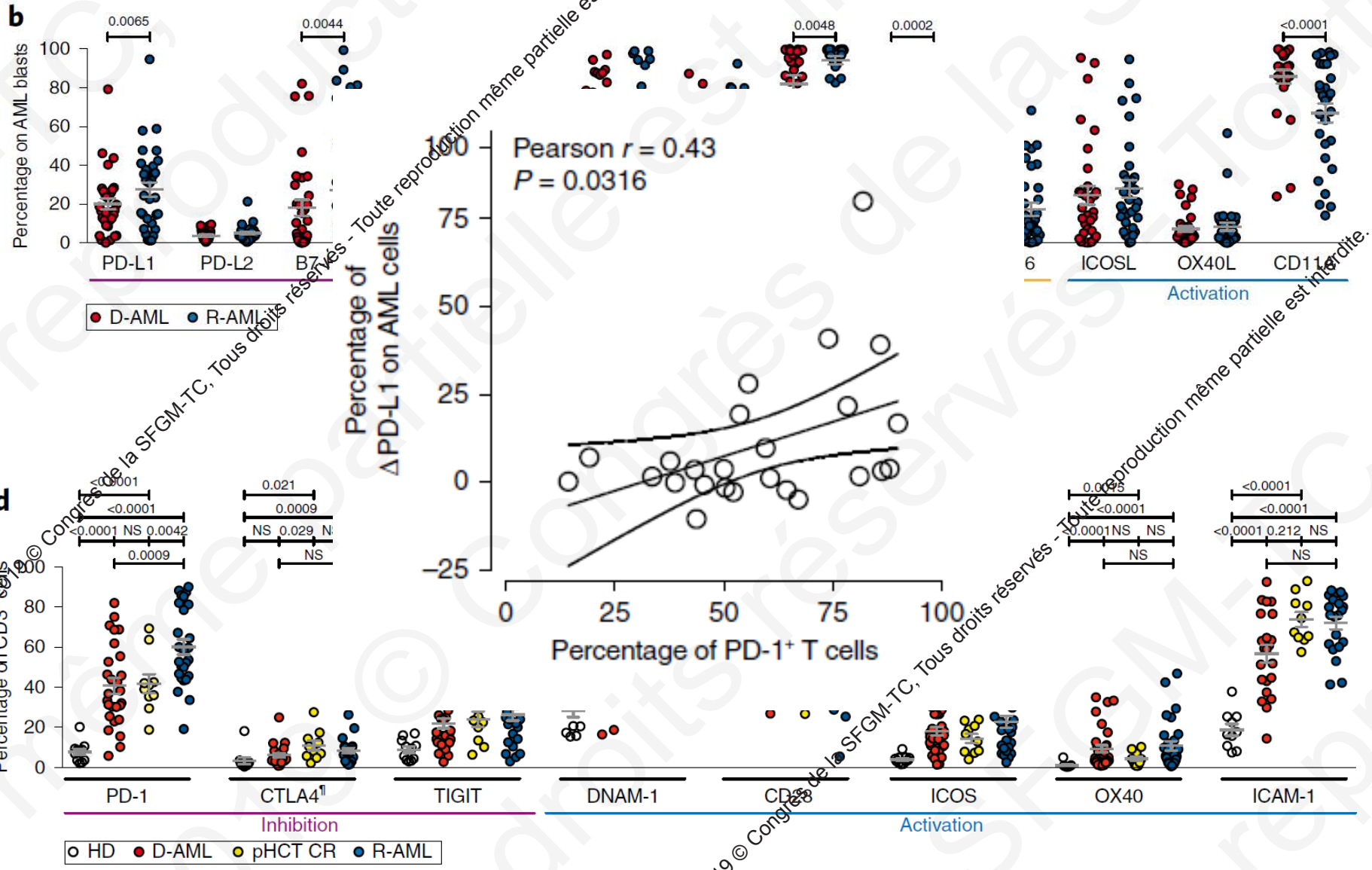
A la rechute post-allogreffe: diminution d'expression des molécules HLA classe II







Rechute post-allogreffe: exhaustion de la réponse T



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Anti-BCMA CAR T-Cell Therapy bb2121 in Relapsed or Refractory Multiple Myeloma

Noopur Raje, M.D., Jesus Berdeja, M.D., Yi Lin, M.D., Ph.D., David Siegel, M.D., Ph.D., Sundar Jagannath, M.D., Deepu Madduri, M.D., Michaela Liedtke, M.D., Jacalyn Rosenblatt, M.D., Marcela V. Maus, M.D., Ph.D., Ashley Turka, Lyh-Ping Lam, Pharm.D., Richard A. Morgan, Ph.D., Kevin Friedman, Ph.D., Monica Massaro, M.P.H., Julie Wang, Pharm.D., Ph.D., Greg Russotti, Ph.D., Zhihong Yang, Ph.D., Timothy Campbell, M.D., Ph.D., Kristen Hege, M.D., Fabio Petrocca, M.D., M. Travis Quigley, M.S., Nikhil Munshi, M.D., and James N. Kochenderfer, M.D.

N=33

MM réfractaires ou en rechute après en médiane 7 lignes de traitement, incluant une autogreffe dans > 90% des cas

Age: 37 à 74 ans

CAR anti-BCMA (Celgene)

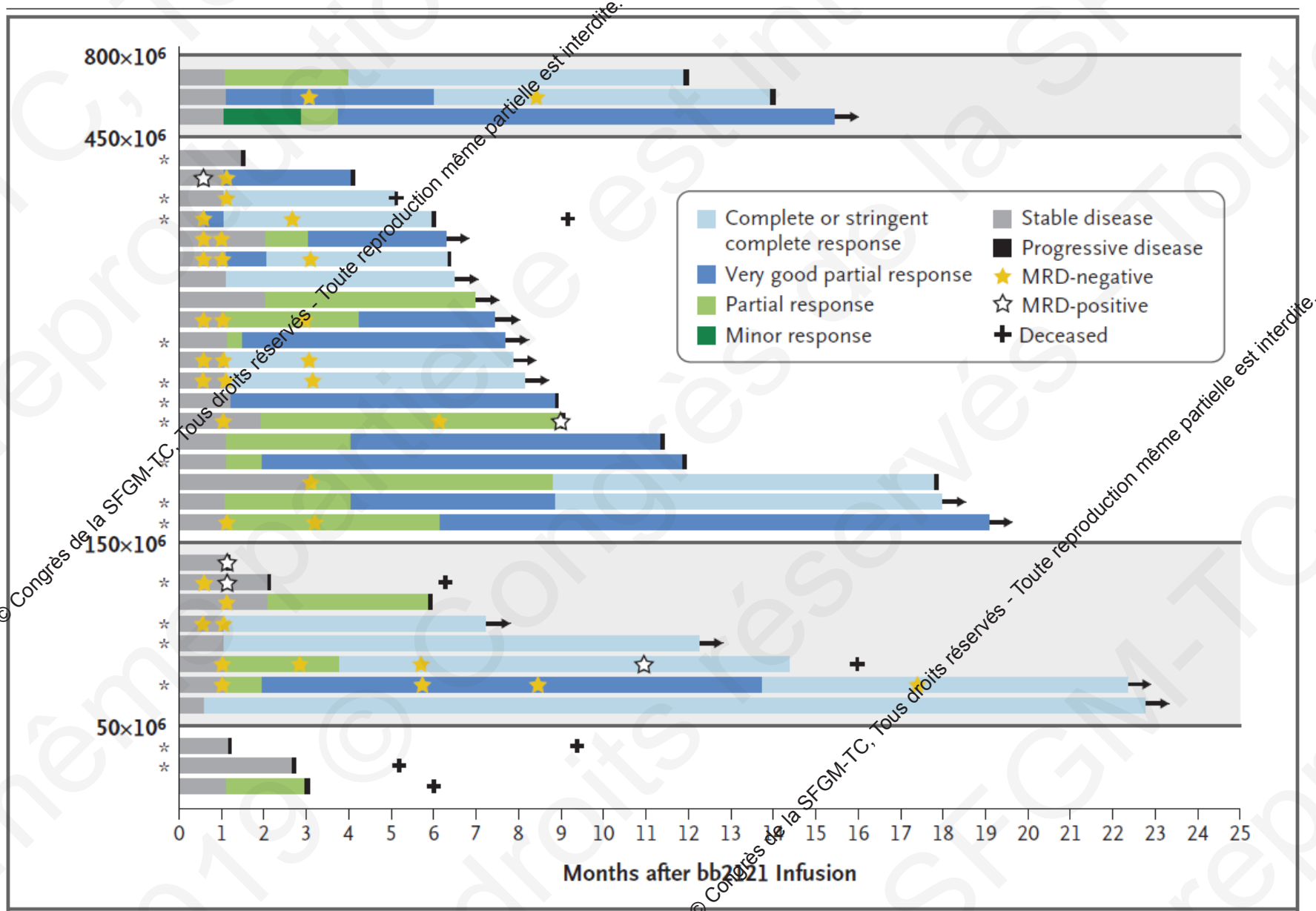


Figure 1. Response to bb2121 Infusion.

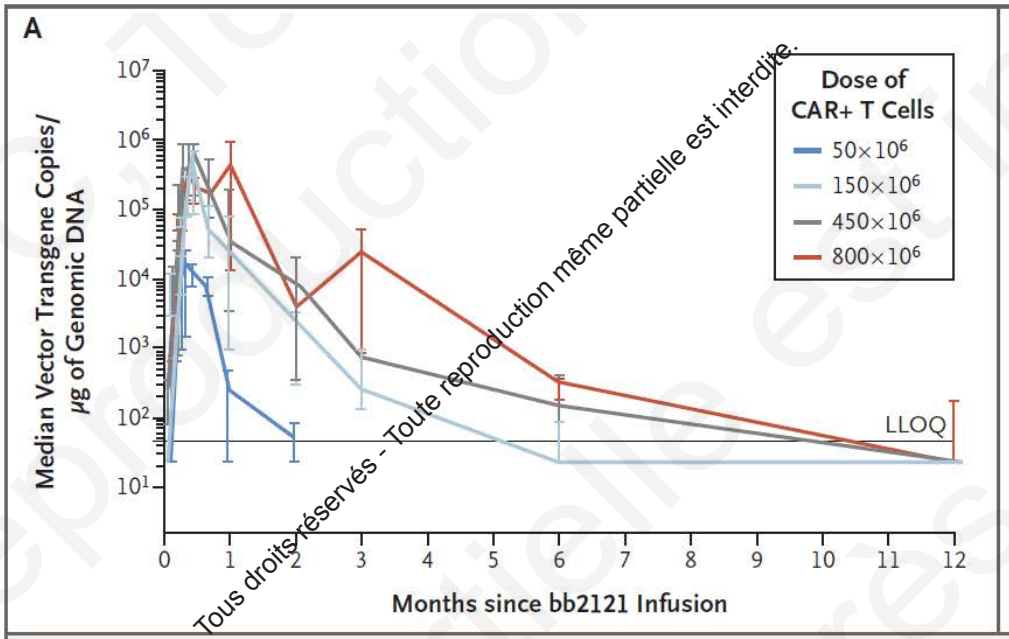
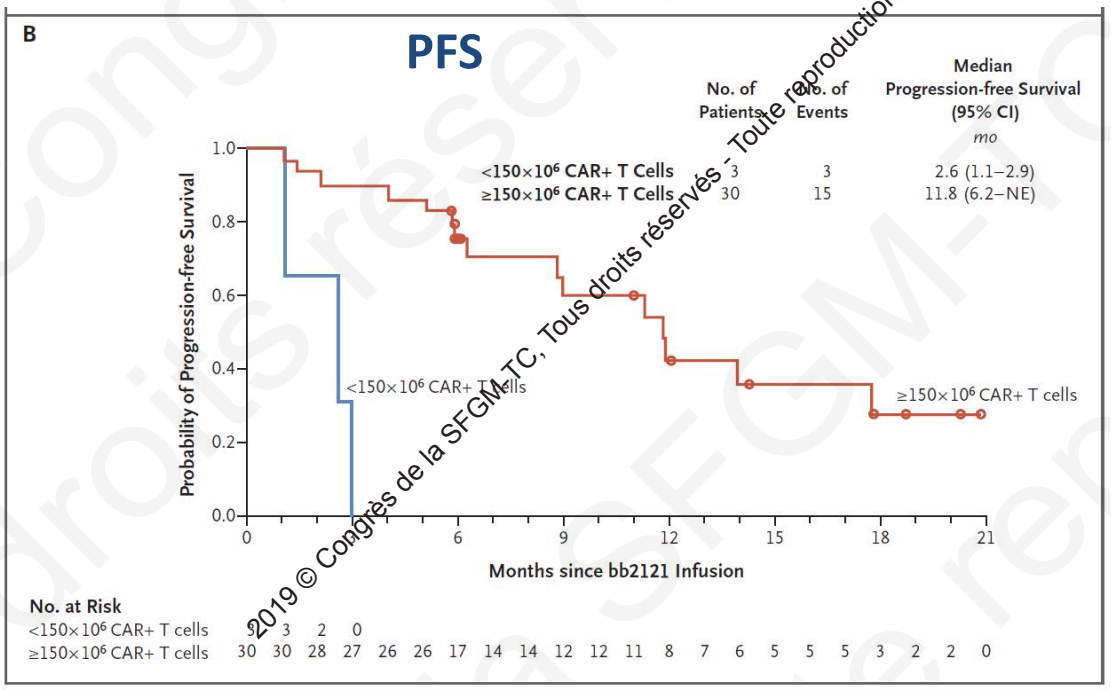


Figure 3. Correlation of CAR T-Cell Expansion with Dose and Response.

Tolérance:

- ✓ 76% CRS (grade < 3 +++)
- ✓ 42% neurotox (un seul grade 4, as de grade 3)



A combination of humanised anti-CD19 and anti-BCMA CAR T cells in patients with relapsed or refractory multiple myeloma: a single-arm, phase 2 trial

Zhiling Yan*, Jiang Cao*, Hai Cheng, Jianlin Qiao, Kuanxin Zhang, Ying Wang, Ming Shi, Jianping Lan, Xiaoming Fei, Lai Jin, Guangjun Jing, Wei Sang, Feng Zhu, Wei Chen, Qingyun Wu, Yao Yao, Gang Wang, Jing Zhao, Junnian Zheng†, Zhenyu Li†, Kailin Xu†

Lancet Haematol 2019

N=25
MM réfractaires ou en rechute après en médiane 6 lignes de traitement

Age: 49 à 61 ans

CAR T produit localement:
CAR T anti-CD19 (10^e6 CAR-T/kg)
CAR anti-BCMA 41-BB (10^e6 CAR-T/kg)

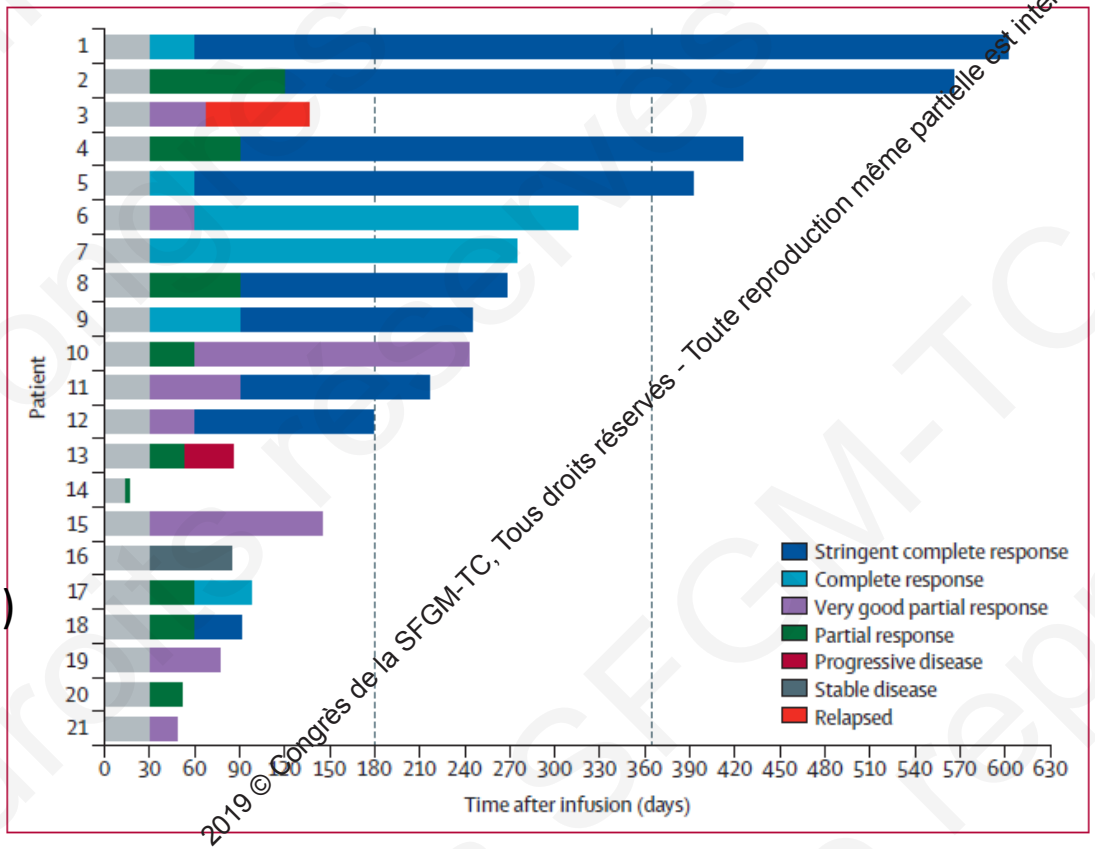
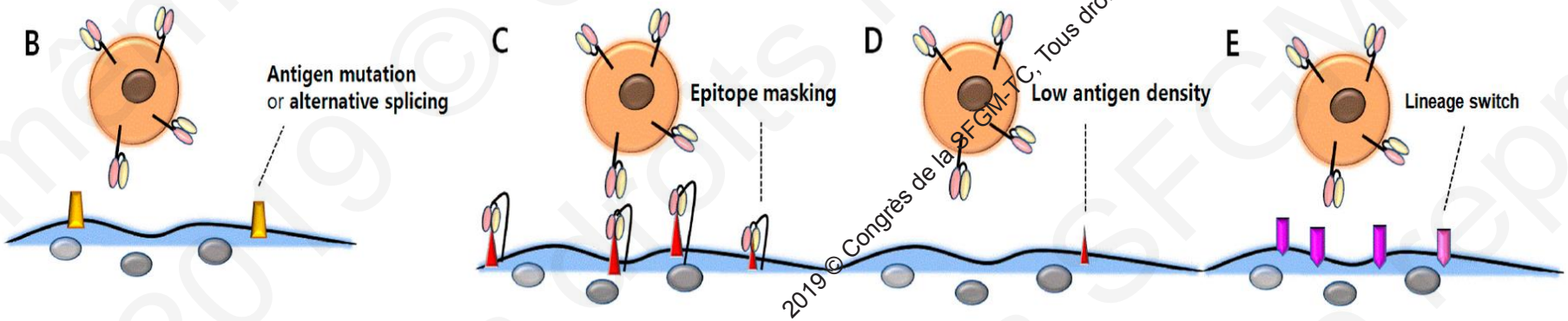


Figure 2: **Response assessment after infusion of CAR T cells**

Echappement / résistance aux CAR-T cells

Study	Patients (*n*)	Response Rate	Relapsed or not Responded Rate	CD19 (-) Relapse Rate (%)
CHOP (Maude et al.)	Pediatric and adult B-ALL (30)	CR, 27 of 30 (90%)	8 of 27 (29.6%)	3 of 27 (11.1%)
ELIANA (Maude et al.)	Pediatric and young Adult B-ALL (75)	CR, 61 of 75 (81%)	17 of 61 (27.9%)	15 of 61 (24.6%)
NCI (Lee et al.)	Pediatric and adult B-ALL (21)	CR, 14 of 21 (66.7%)	7 of 14 (50%)	2 of 14 (14.3%)
SCRI (Gardner el al.)	Pediatric and adult B-ALL (7)	CR, 100%	2 of 7 (28.6%)	2 of 7 (28.6%), lineage-witch
MSKCC (Park et al.)	Adult B-ALL (53)	CR, 44 of 53 (83%)	25 of 44 (57%)	4 of 44 (9%)
FHCRC (Turtle et al.)	Adult B-ALL (29)	CR, 27 of 29 (93%)	9 of 27 (33.3%)	2 of 27 (7.4%)
ZUMA-1 (Neelapu et al.)	DLBCL, PMBCL, tFL (111)	ORR, 82 % (CR, 54%)	52 of 111 (46.8%)	3 of 11 analyzed (27.2%)
Schuster et al.	DLBCL, FL (28)	ORR, 52 % (CR, 40%)	5 of 28 (17.9%)	1 of 5 analyzed, (20%)
Jacobson et al.	Aggressive B-NHL (73)	ORR, 57 % (CR, 36%)	Unknown	1 of 4 analyzed, (25%)
Oak et al.	DLBCL, PMBCL, tFL (22)	ORR, 86 % (CR, 45.5%)	5 (22.7%)	2 of 4 analyzed, (50%)



Int. J. Mol. Sci. **2019**, *20*, 5010

DUAL ou MULTI CAR-T cells

TABLE 1 | Actively recruiting ClinicalTrials.gov registered studies using tandem CARs or administration of multiple single CARs.

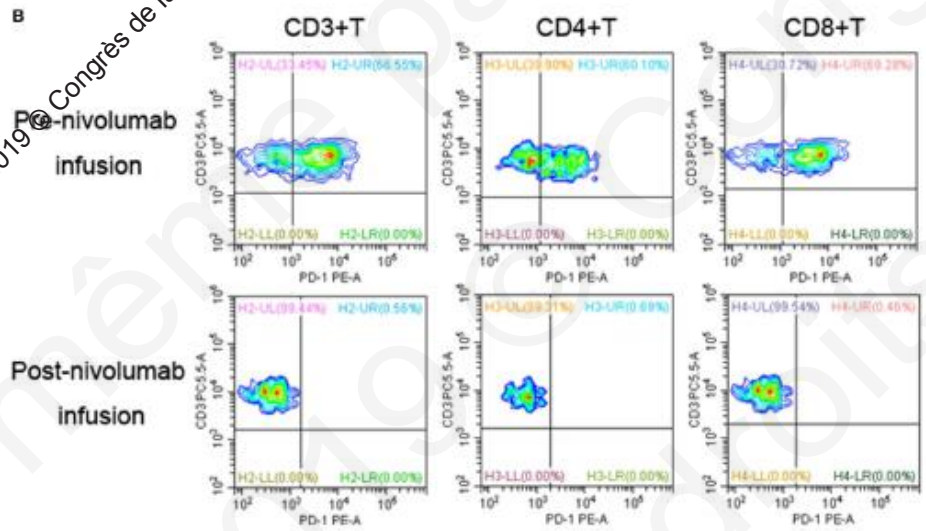
CAR	NCT number	B cell malignancy	Site
Sequential CD19, CD20	NCT03207178	Non-specified	Shanghai, China
Multiple mixtures (CD19 + CD22, CD38, CD20, CD123, CD70, or CD30)	NCT03125577	Non-specified	Guangzhou, Shenzhen & Kunming, China
"Armored" CD19	NCT03085173	CLL	New York, NY, USA
CD19–CD20 dual	NCT03398967	Leukemia, Lymphoma	Beijing, China
	NCT03019055	Lymphoma, CLL	Milwaukee, WI, USA
CD19–CD22 dual	NCT03614858	Leukemia	Suzhou, China
	NCT03593109	Lymphoma	Xi'an, China
	NCT03468153	Lymphoma	Shanghai, China
	NCT03448393	Leukemia, Lymphoma	Bethesda, MD, USA
	NCT03398967	Leukemia, Lymphoma	Beijing, China
	NCT03330691	Leukemia, Lymphoma	Seattle, WA, USA
	NCT03289455	Leukemia	London & Manchester, UK
	NCT03287817	Lymphoma	London, Manchester & Newcastle, UK
	NCT03241940	Leukemia	Palo Alto, CA, USA
	NCT03233854	Lymphoma	Palo Alto, CA, USA

frontiers in Oncology

ORIGINAL RESEARCH
published: 19 August 2019
doi: 10.3389/fonc.2019.00767

Anti-CD19 Chimeric Antigen Receptor T Cells in Combination With Nivolumab Are Safe and Effective Against Relapsed/Refractory B-Cell Non-hodgkin Lymphoma

Yaqing Cao[1†], Wenyi Lu[2†], Rui Sun[1], Xin Jin[3], Lin Cheng[1], Xiaoyuan He[3], Luqiao Wang[1], Ting Yuan[2], Cuicui Lyu[2] and Mingfeng Zhao[2]*



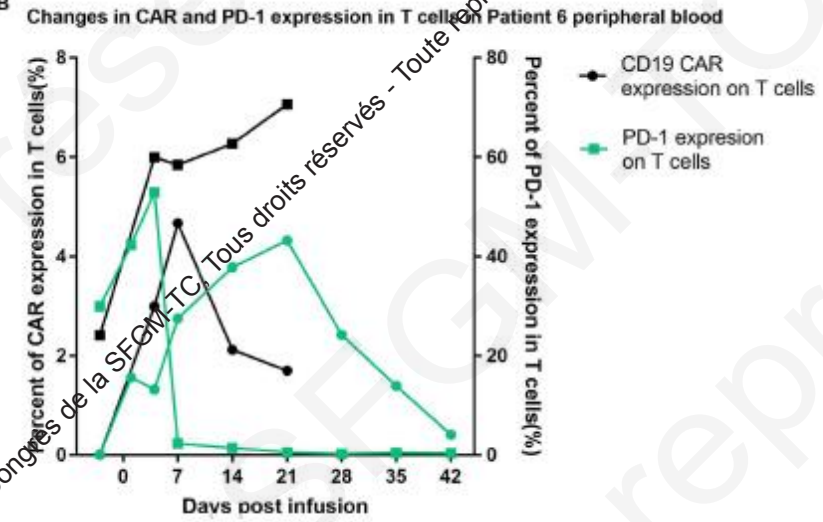


TABLE 2 | Patient response and toxicity.

Patient no.	Disease status at study entry	Conditioning regimen before T cell infusion	No. of CAR-positive T cells infused (10^6/kg)	Response		CRS grade	Grade 3 toxicities (excluding CRS)
				Type	Duration		
1	PD	FC	8	PR	5	1	None
2	PD	FC	10	PR	5	2	None
3	PD	FC	5	PR	6	2	Febrile neutropenia, anemia, neutropenia, thrombocytopenia
4	PD	FC	11	NR	/	None	None
5	PD	FC	6	CR	14+	1	None
6	PD	FC	11	CR	13+	None	None
7	PD	FC	8	CR	9	2	Gamma glutamyl transpeptidase level increased, febrile neutropenia, anemia, neutropenia, thrombocytopenia
8	PD	FC	8	CR	6+	1	None
9	PD	FC	11	PR	1	2	Gamma glutamyl transpeptidase level increased
10	PD	FC	6	CR	1	2	Heart failure, thrombocytopenia
7	PD	FC	5	NR	/	2	Febrile neutropenia, neutropenia

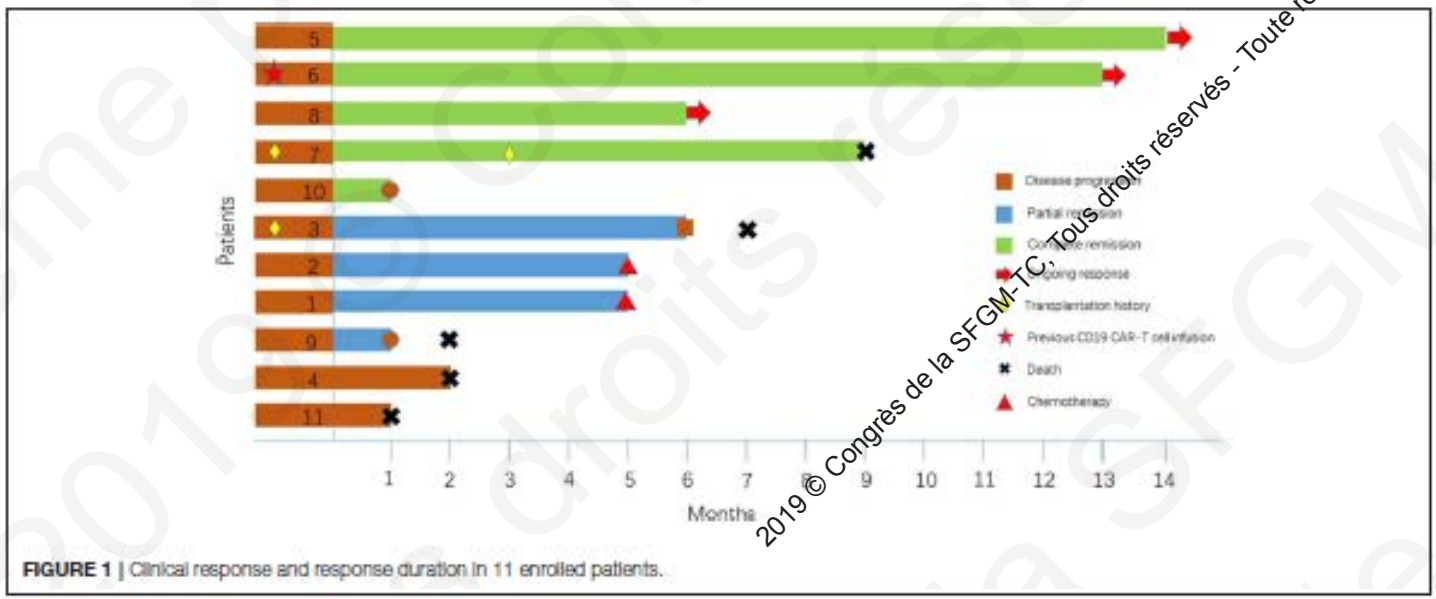


FIGURE 1 | Clinical response and response duration in 11 enrolled patients.

Received: 8 July 2019 | Revised: 14 August 2019 | Accepted: 15 August 2019

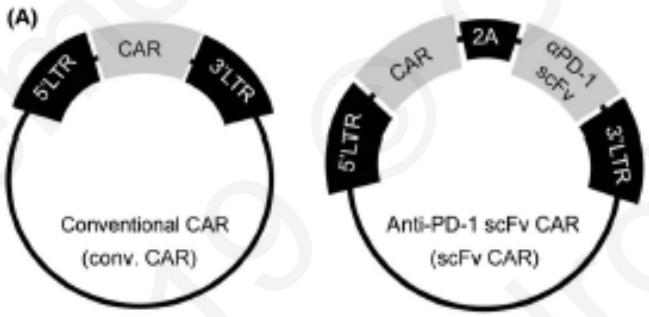
DOI: 10.1111/cas.14169

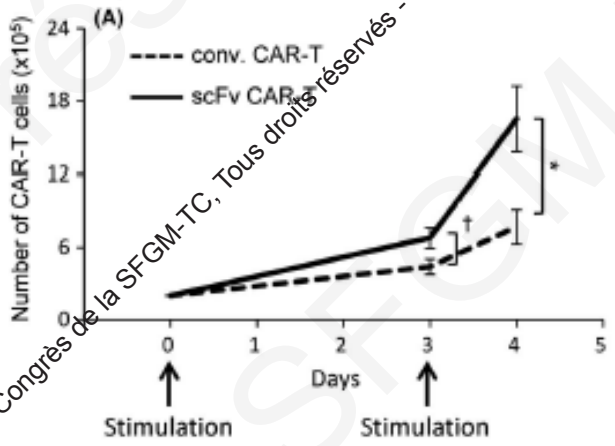
ORIGINAL ARTICLE

Cancer Science WILEY

Improved survival of chimeric antigen receptor-engineered T (CAR-T) and tumor-specific T cells caused by anti-programmed cell death protein 1 single-chain variable fragment-producing CAR-T cells

Masaaki Nakajima[1,2] | Yukimi Sakoda[1] | Keishi Adachi[1] | Hiroaki Nagano[2] | Koji Tamada[1]



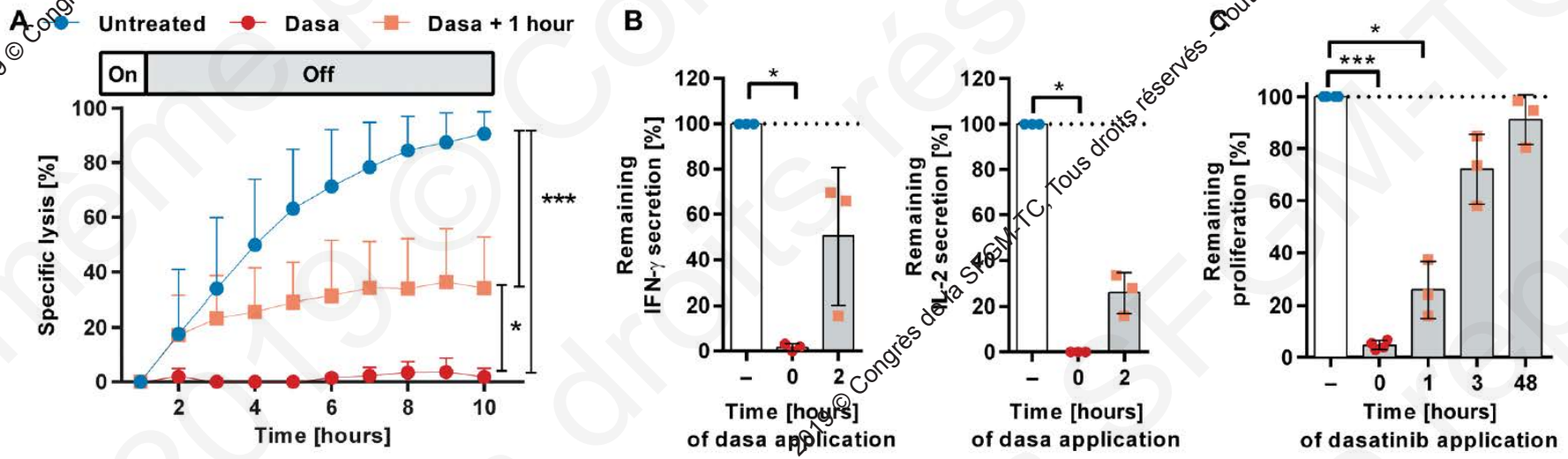


CANCER

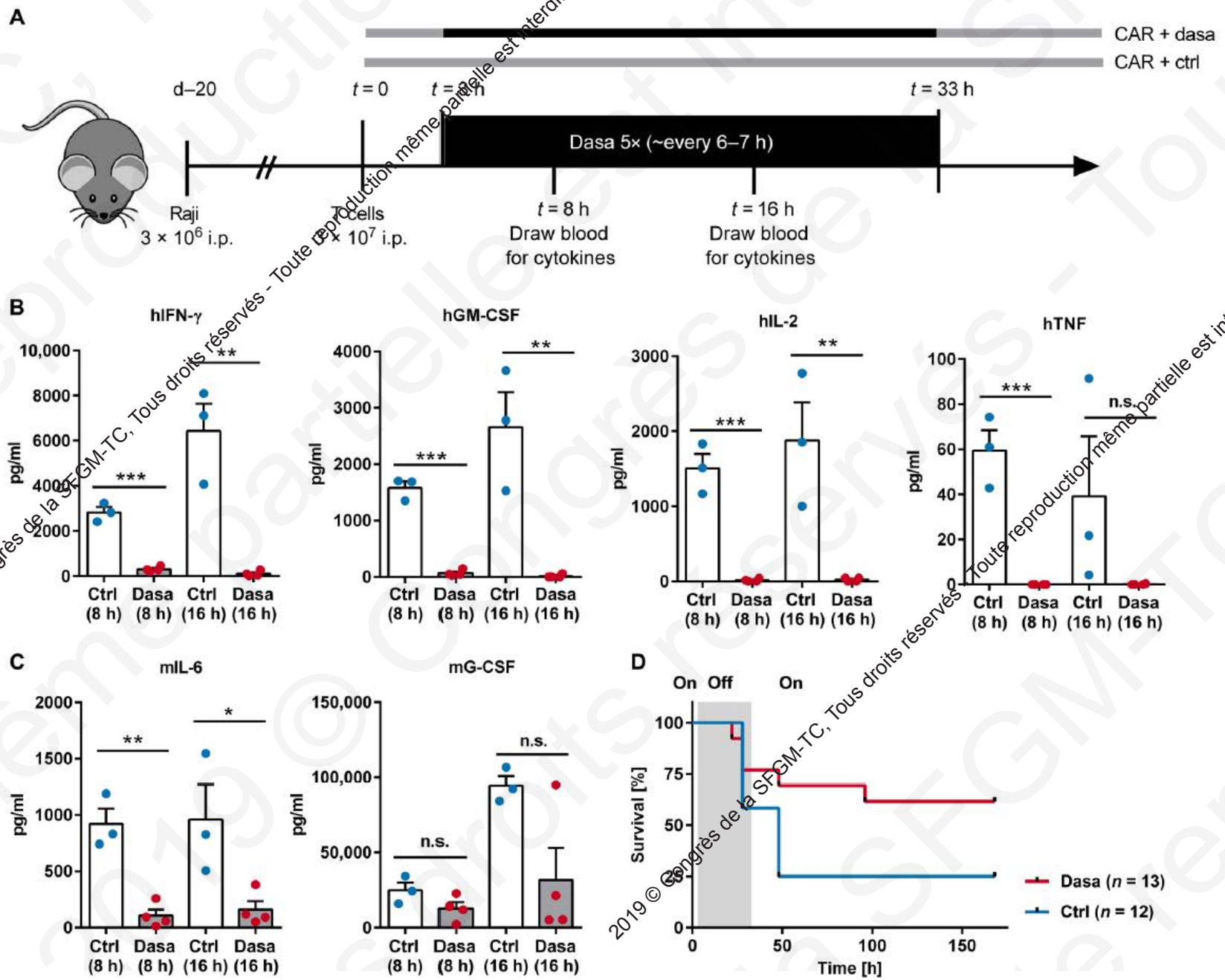
The tyrosine kinase inhibitor dasatinib acts as a pharmacologic on/off switch for CAR T cells

Katrin Mestermann[1], Theodoros Giavridis[2], Justus Weber[1], Julian Rydzek[1], Silke Frenz[1], Thomas Nerreter[1], Andreas Mades[1], Michel Sadelain[2], Hermann Einsele[1], Michael Hudecek[1]*

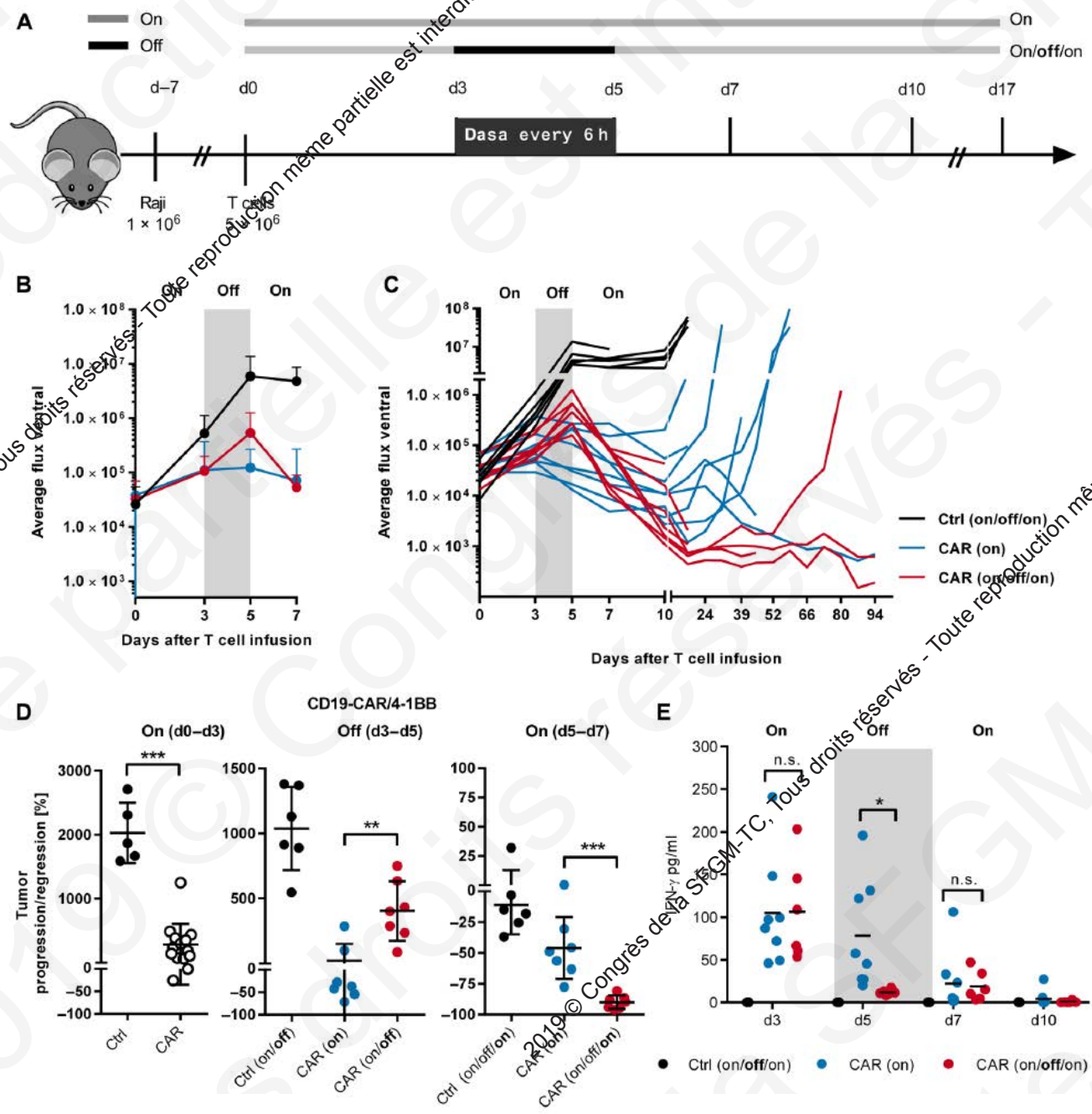
Mestermann K. *et al.*, *Sci. Transl. Med.* **11**, eaau5907 (2019) 3 July 2019



Le dasatinib administré de H3 à H33 post-CAR-T permet de contrôler le CRS



Le dasatinib administré de J3 à H5 post-CAR-T: effet suspensif sur l'efficacité du CAR-T



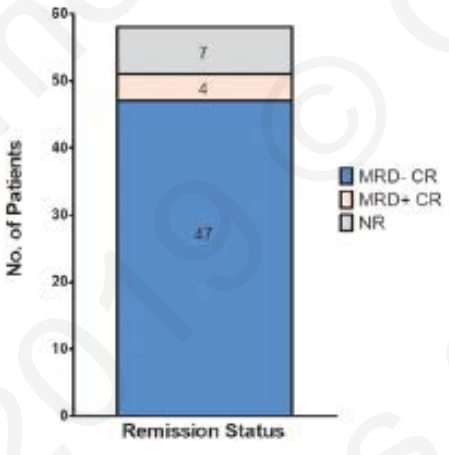
Received: 28 June 2019 | Revised: 12 July 2019 | Accepted: 13 July 2019

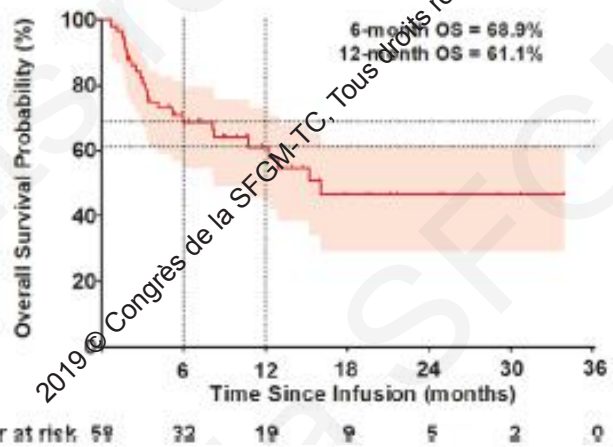
DOI: 10.1002/ajh.25582

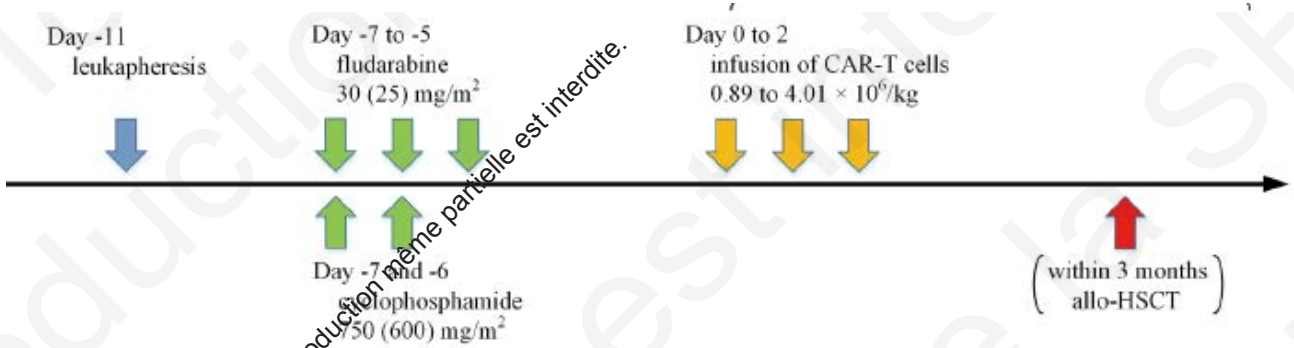
RESEARCH ARTICLE

Anti-CD19 chimeric antigen receptor-modified T-cell therapy bridging to allogeneic hematopoietic stem cell transplantation for relapsed/refractory B-cell acute lymphoblastic leukemia: An open-label pragmatic clinical trial

Huiwen Jiang[1,2] | Chenggong Li[1,2] | Ping Yin[3] | Tao Guo[1,2] | Lin Liu[1] | Linghui Xia[1] | Yaohui Wu[1,2] | Fen Zhou[1,4] | Lisha Ai[1] | Wei Shi[1] | Xuan Lu[1] | Huafang Wang[1] | Lu Tang[1,2] | Qiuzhe Wei[1] | Jun Deng[1,2] | Runming Jin[1,4] | Wei Xiong[2] | Jian Dong[2] | Heng Mei[1,2*] | Yu Hu[1,2*]







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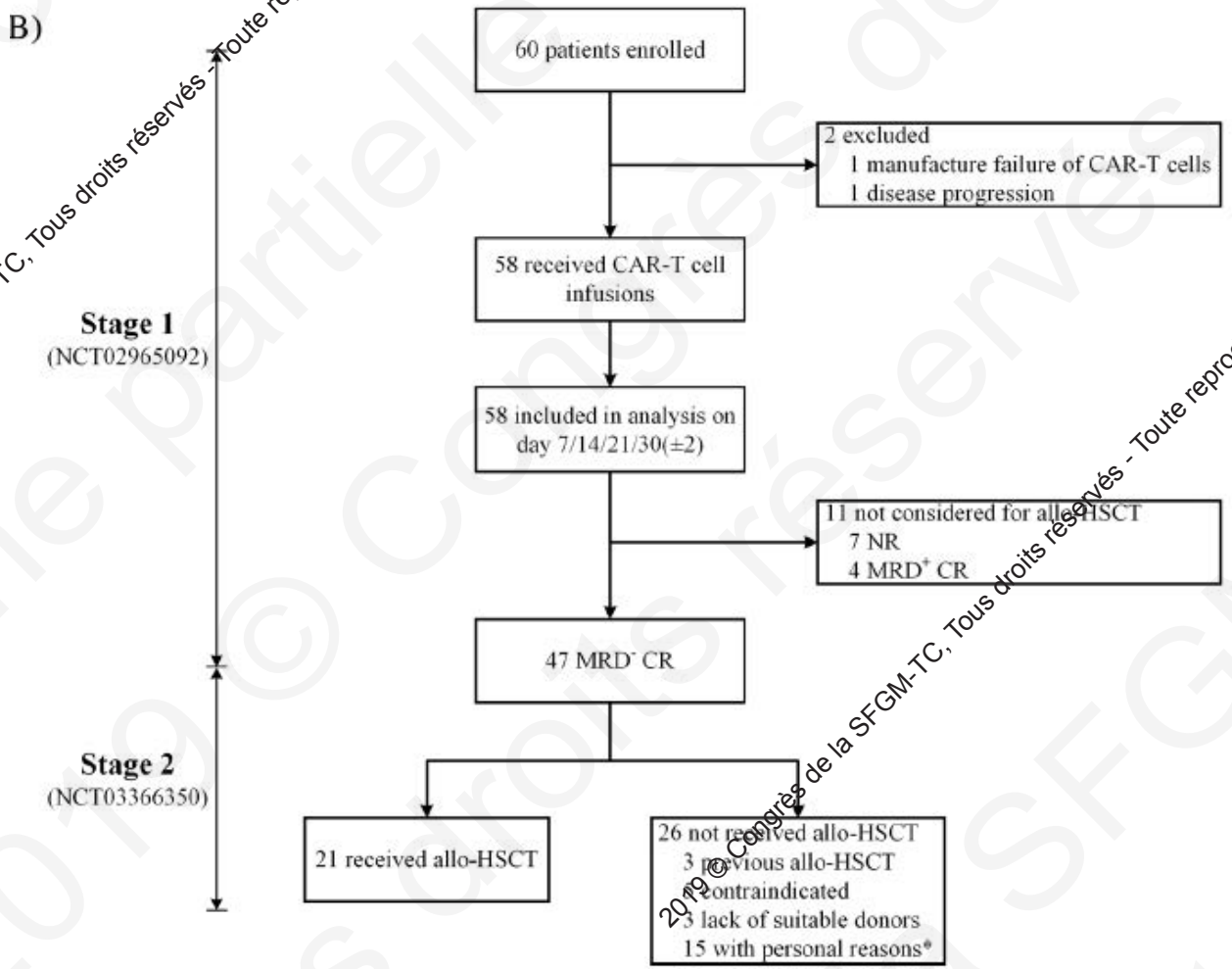
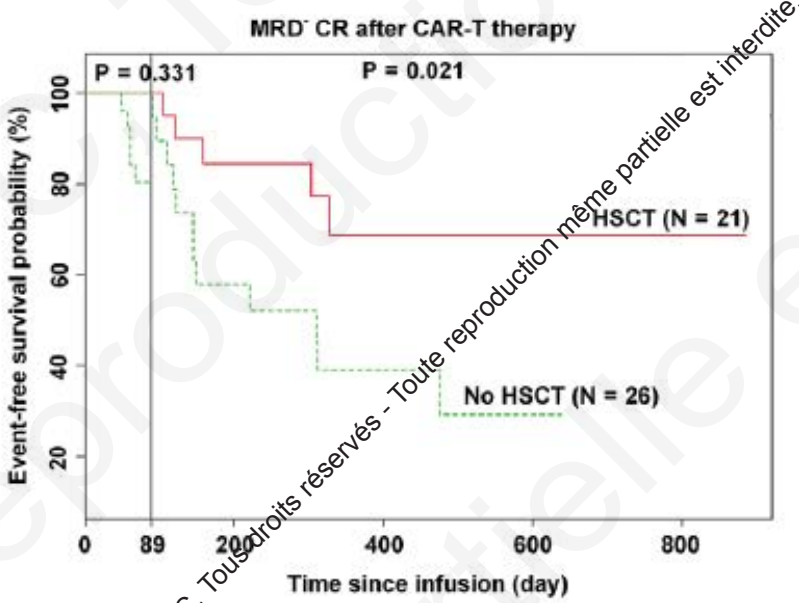
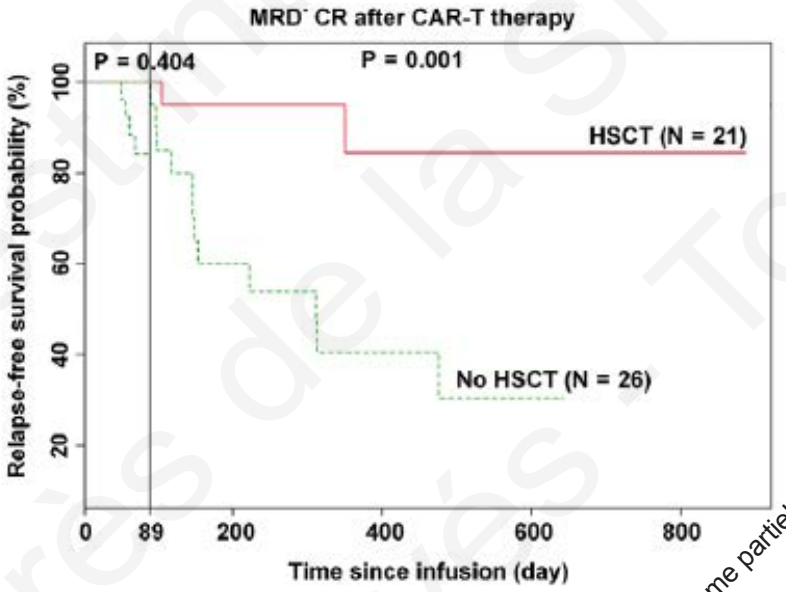
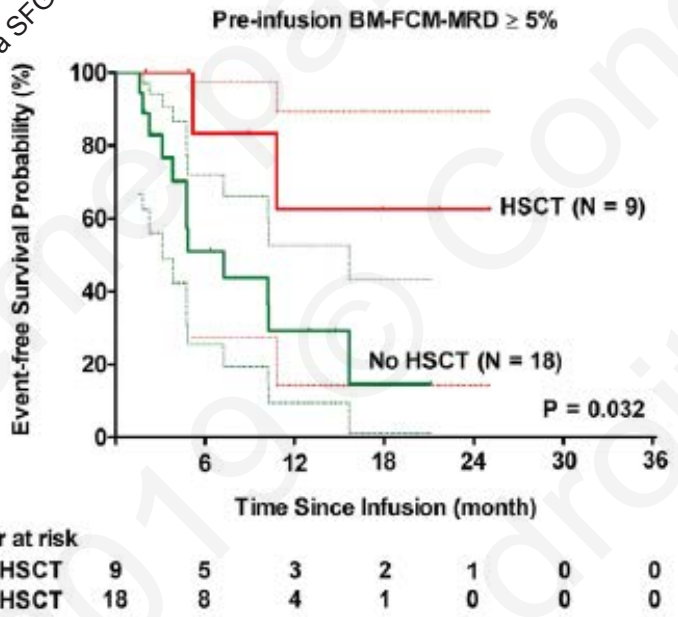
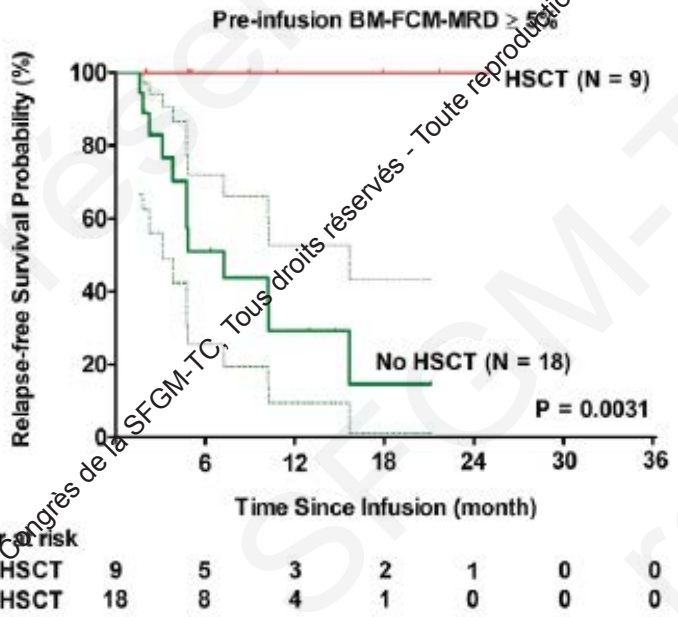
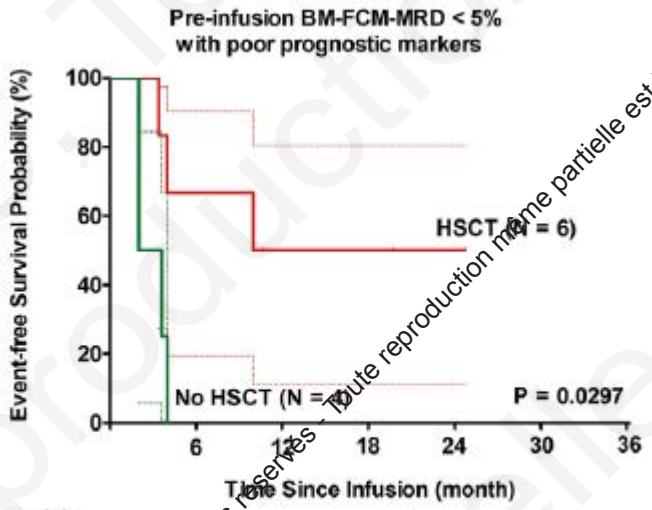


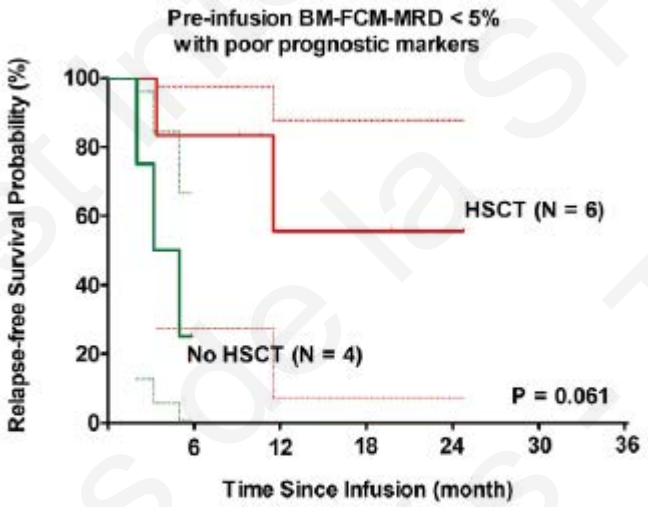


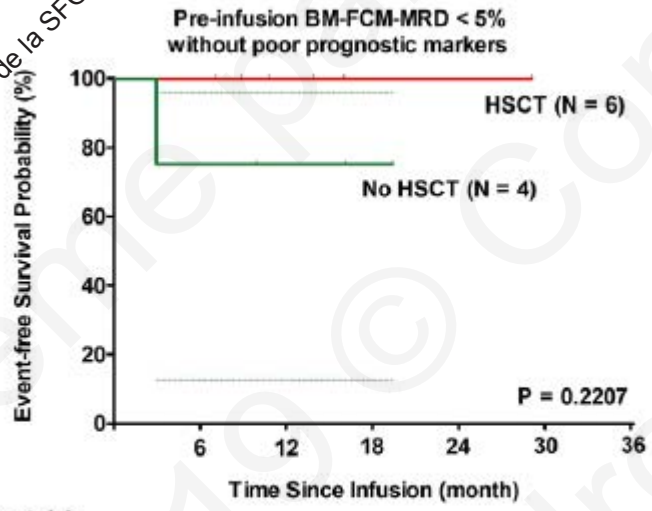


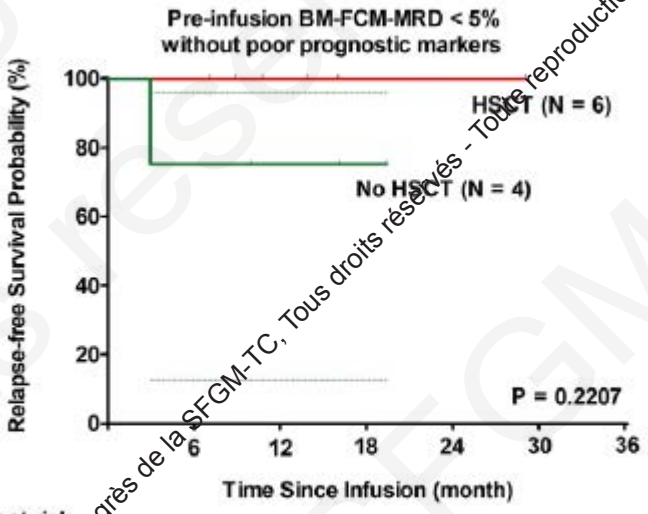








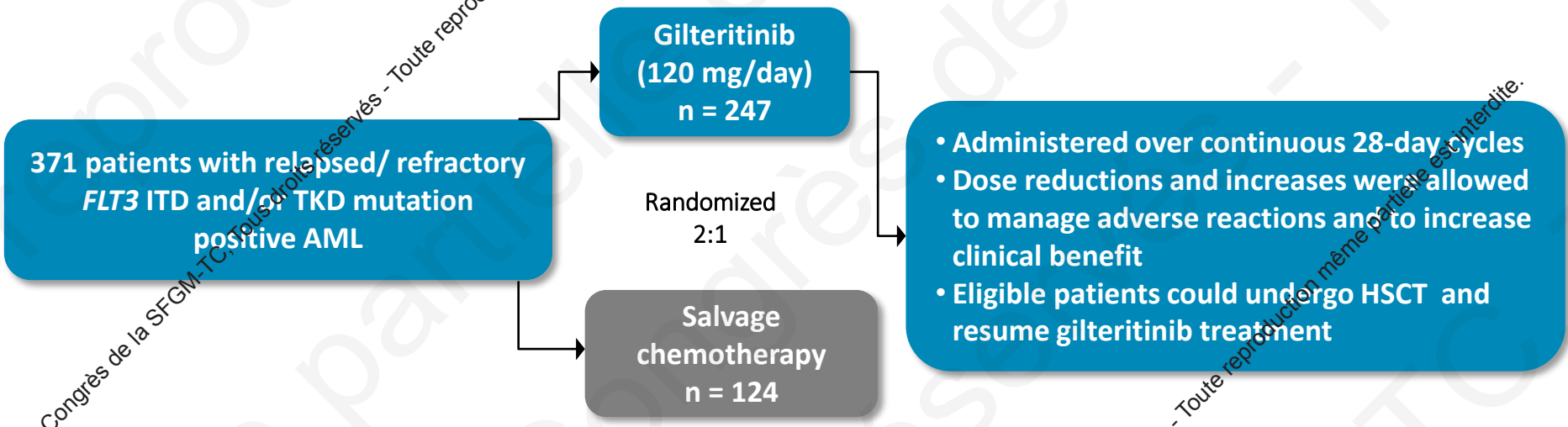




Caryotype complexe
BCR-ABL
MLL-AF4
TP53
E2A-PBX1

ADMIRAL: Study Design

Phase 3, open-label, multicenter, randomized study of gilteritinib versus salvage chemotherapy in patients with relapsed/refractory AML with *FLT3* mutation



Co-primary endpoints:

- OS of gilteritinib versus salvage chemotherapy
- Rate of Complete Remission (CR) and Complete Remission with partial Hematologic recovery (CR_h) [CR/CR_h] following gilteritinib treatment

Post-treatment follow-up:
- end-of-treatment visit within 7 days of treatment discontinuation
- 30-day safety follow-up
- long-term follow-up visits (every 3 months for up to 3 years)

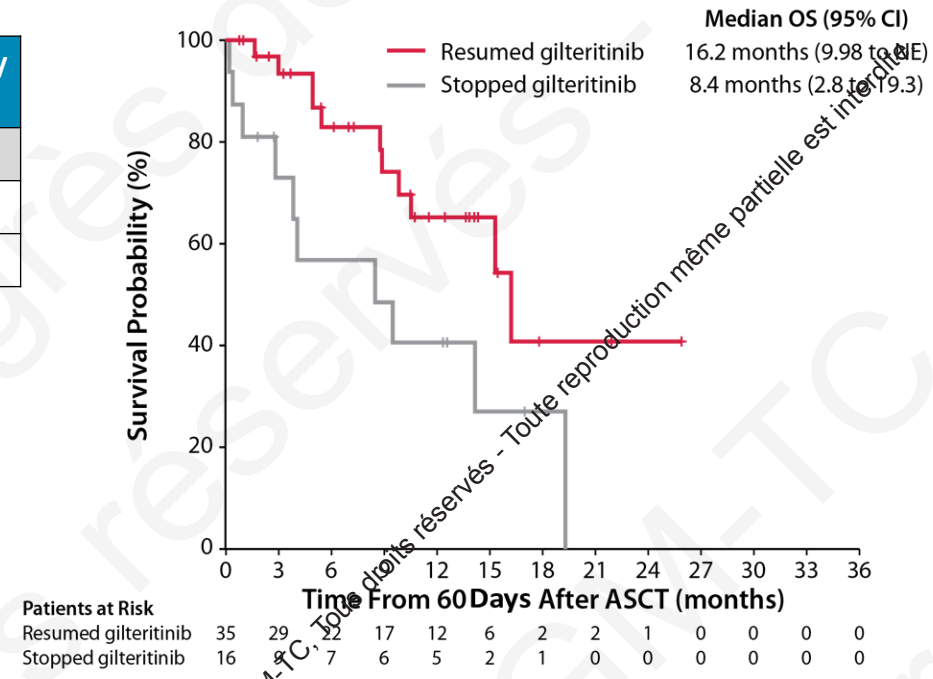
NE Perl.N Engl J Med. 2019 Oct 31;381(18):1728-1740.

ADMIRAL - Efficacy Results: HSCT

Response Parameter*	Gilteritinib (n = 247)	Salvage Chemotherapy (n = 124)
CR, n (%)	52 (21%)	13 (11%)
CR/CR_h, n (%)	84 (34%)	19 (15%)
Allogeneic HSCT, n (%)	63 (26%)	19 (15%)

HSCT, Haematopoietic Stem Cell Transplantation; ASCT, Allogeneic Stem Cell Transplantation

Non-Randomised Landmark Analysis from Day 60 Post-HSCT of Survival in the Gilteritinib Arm[1.11] (NOT STATISTICALLY SIGNIFICANT)



A median OS of 16.2 months for patients who resumed Gilteritinib versus 8.4 months for those who did not resume. The magnitude of the signal from this analysis suggest the patients who resumed Gilteritinib post-HSCT may benefit versus those who did not resume

AE Perl.N Engl J Med. 2019 Oct 31;381(18):1728-1740.

MERCI POUR VOTRE ATTENTION !

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