# Actualités de la greffe et la thérapie cellulaire

Revue de la littérature

2020-2021

# 2020: a year in review

**While one health issue has dominated the news in 2020, Farhat Yaqub looks back at some of the year's most important non-COVID-19 stories in health and medicine**


For more on **racism in medicine** see *Perspectives* Lancet 2020; 396: 1645–48

For more on the **explosions in Beirut** see *Viewpoint* Lancet 2020; 396: 1280–82

For more on **Yemen** see *World Report* Lancet 2020; 395: 930

For more on **Syria** see *World Report* Lancet 2020; 395: 855–58

For more on **fires in Australia** see *Editorial* Lancet 2020; 395: 1615

For more on **fires in the USA** see *World Report* Lancet 2020; 396: 1545–47

For more on **assisted suicide in Germany** see *World Report* Lancet 2020; 395: 771

For more on **legalised euthanasia in New Zealand** see *World Report* Lancet 2020; 396: 1018

For more on the **commitment to eliminate cervical cancer** see https://who.int/news-room/q-a-detail/2020-a-cervical-cancer-free-future-first-ever-global-commitment-to-eliminate-a-cancer

## Black Lives Matter

In the USA, the killing of George Floyd by police officers on May 25 reignited the Black Lives Matter movement on a global scale. In response, many medical institutions and science, technology, and medical journals rushed to decry racism and pledged to address it. In October, the US Pharmaceutical Research and Manufacturers of America Board committed to enhance the diversity of participants in clinical trials to help reduce disparities in health care. This principle, which will be effective from April 14, 2021, acknowledged some of the past explorations and mistreatments of Black people in medicine including the 1932–72 Tuskegee syphilis study and the cancer cells taken from Henrietta Lacks in 1951 without her knowledge and used for research.

## Ebola epidemics

On June 25, the tenth outbreak of Ebola virus disease in eastern Democratic Republic of the Congo, which occurred amid conflict, was declared over, after nearly 2 years. It was the second largest outbreak in history. More than 303 000 individuals were vaccinated with rVSV-ZEBOV-GP. Preparedness in the neighbouring countries helped to prevent the outbreak becoming bigger. But this success story was marred by controversy: 51 women alleged sexual abuse by mostly foreign aid workers. On Oct 15, WHO announced an Independent Commission to establish the facts, identify and support survivors, stop any ongoing abuse, and hold the perpetrators to account. Just as the tenth outbreak was waning, outbreak number 11 was declared on June 1 in the western part of the country, Equateur Province. This outbreak was declared over on Nov 18.

## Africa polio-free

On Aug 25, the WHO African region (representing 47 countries) was certified as being free from wild poliovirus by the Africa Regional Certification Commission: no cases have been reported in this region for 4 years. With ongoing transmission in Afghanistan and Pakistan, the Eastern Mediterranean Region remains the only WHO region that is not free of wild poliovirus.

## Beirut explosion

Even before the explosion in Beirut's port on Aug 4, Lebanon was a country under strain: there was an economic crisis, high inflation, political corruption, huge numbers of Syrian refugees, and the COVID-19 pandemic (which first appeared in Lebanon in February). The explosion killed more than 200 people, resulted in about 6500 people being hospitalised with moderate to critical injuries, and left 145 000 needing psychological support. It also destroyed infrastructure, leaving more than 31 000 houses uninhabitable. The cost of the damage was US$15 billion. The explosion damaged 17 hospitals (four severely) and 16 primary health-care centres; patients in three of the severely damaged hospitals had to be transported elsewhere. 99% of medical supplies are imported, and the blast destroyed a shipment of personal protective equipment and damaged warehouses where vaccines and medicines were stored. Because of shortages in medicines, most hospitals have had to close departments. In December, Lebanon's caretaker prime minister and three former ministers were charged with negligence for failing to respond to warnings about the unsafe storage of ammonium nitrate at the port.

## Yemen and Syria

The humanitarian crisis in Yemen continued, exacerbated by the worsening conflict and economic torrential rains and flooding, COVID-19, and a fuel crisis. More than 80% of the population (an estimated 24·1 million people) are in need of assistance, and 14·4 million are in acute need. Cases of acute malnutrition increased by nearly 10% in the south.

With the ongoing conflict in Syria, more than 11 million people are in need of humanitarian assistance, but only 7·4 million have been receiving aid from humanitarian agencies each month. As of November, 6·7 million people were internally displaced and a third of these were living in damaged buildings or in public spaces. People are unable to feed their families because of the devalued Syrian currency and rising food prices, and in October the government introduced limits on the amount of subsidised bread per person that could be bought at bakeries. Health services are stretched because of the COVID-19 pandemic and there are shortages in medical personnel and medical supplies. If all this was not too much already for the people in Syria, fires in October damaged or destroyed homes and agricultural land, and affected power and water supplies and access to hospitals; an estimated 140 000 people (28 000 households) were affected.

## Fires in Australia and the USA

Fires in Australia and the USA resulted in excess deaths, hospitalisations, emergency department visits, and psychological, respiratory, cardiovascular, and cerebrovascular effects, and are likely to have longer-term health effects.

Australia's bushfire season peaked in January; 33 people died as a direct result of the bushfires. 400 megatonnes of carbon dioxide were released into the atmosphere in early January, equal to 75% of the country's industry emissions in 2018–19. Smoke from the bushfires drifted as far as Argentina and Chile by Jan 6. The smoke-related health costs of this bushfire season were estimated to be AU$1·95 billion—nine times higher than the median of the previous 19 bushfire seasons.

From Jan 1 to Dec 4, more than 52 000 wildfires were recorded in the USA. People had to evacuate their homes because of wildfires in the west coast, which was smothered in heavy smoke. Arizona, California, Colorado, Nevada, New Mexico, and Utah had the hottest August on record. In August, lightning strikes started more than 900 wildfires in California, and as of Dec 4 six large fires are still burning.

## Opioid crisis

In October, OxyContin's manufacturer, Purdue Pharma, reached a settlement of US$8·3 billion with the US Department of Justice over its role in the opioid crisis. The settlement was approved by a federal bankruptcy judge in November. Purdue Pharma also agreed to plead guilty to three federal criminal charges for its role in the country's opioid crisis. Purdue Pharma and members of the Sackler family, who own the company, have been aggressively marketing opioids since the 1990s. The company filed for bankruptcy in 2019 and is likely to be organised into a public benefit corporation, with profits expected to be used for programmes to alleviate the opioid crisis. Also in October, Walmart filed a pre-emptive lawsuit against the Department of Justice (which was threatening to sue the retailer) and the Drug Enforcement Administration to seek clarification of the legal responsibilities of all pharmacists in filling opioid prescriptions.

## Cervical cancer commitment

On Nov 17, WHO announced the Global Strategy to Accelerate the Elimination of Cervical Cancer, with 194 countries committing to eliminate this cancer. Its targets are to have 90% of girls fully vaccinated with the human papillomavirus vaccine by age 15 years, 70% of women screened with a high-performance test by age 35 years and again by age 45 years, and treatment for 90% of women who need it by 2030. Meeting these goals will put countries on the path to eliminating cervical cancer and more than 40% of new cases and 5 million related deaths will be prevented by 2050. As well as saving lives, the economic returns could be substantial, through increases in women's workforce participation and the benefits of women's improved health on their families, communities, and societies.

## Assisted dying laws

In February, a German court rejected a 2015 law banning professionally assisted suicide as being unconstitutional. The 2015 law was to prevent assisted dying becoming a business, whereby people would pay for help to die, and the punishment for breaking this law could be a 5-year jail sentence. In April, the supreme court in The Hague, Netherlands, approved euthanasia for patients with severe dementia who have unbearable and endless suffering, if they have provided a written request before they lose the ability to express their will as a result of advanced dementia. This ruling comes after a doctor was prosecuted and acquitted for euthanising a woman with severe Alzheimer's disease. In October, New Zealand voted to legalise euthanasia; this law is expected to come into effect next November. Two of the criteria for assisted dying in New Zealand will be a life expectancy of less than 6 months because of a terminal illness and the ability to make an informed decision.

## Inappropriate behaviour accusations

On social media, former employees made allegations against the global advocacy group Women Deliver that included racism, discrimination, microaggressions, verbal abuse, toxic behaviour, and white faux feminism. In June, Women Deliver's Board of Directors commissioned an independent investigation into allegations of racial discrimination. One of the report's key findings was that Women Deliver had "undergone a period of rapid growth, during which its policies and practices lagged behind, which may have potentially left opportunity for bias in implementation".

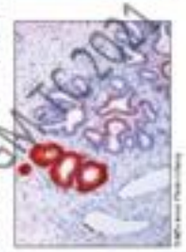
In September, allegations of bullying and harassment of employees and creating a poisonous work environment were made against the Executive Director of the Stop TB Partnership, Lucica Ditiu. Stop TB commissioned an independent external review, and in November released an action plan in response to the review. Stop TB stated in this plan: "Any form of racism or workplace misconduct is unacceptable and inconsistent with the values of the Stop TB Partnership...Where any of us has been at fault in this, the fight against TB suffers."

## Second HIV patient cured

On March 10, *The Lancet HIV* reported that a second patient had been cured of HIV after a CCR5Δ32/Δ32 allogeneic haematopoietic stem-cell transplantation. The London patient, 40-year-old Adam Castillejo, was still in remission 30 months after analytical treatment interruption. Castillejo's HIV load in the plasma remained undetectable. Replication-competent HIV was also not detectable in the CSF, intestinal tissue, or lymphoid tissue.

Timothy Brown (the Berlin Patient) died on Sept 29, 2020, at the age of 54 years, after a recurrence of his leukaemia. Brown was the first person to be cured of HIV, in 2007, after receiving a stem-cell transplant when his leukaemia rebounded despite chemotherapy. He became an advocate of HIV cure research.

*Farhat Yaqub*



For more on **allegations against Women Deliver** see *World Report* Lancet 2020; 396: 1477

For more on **alleged inappropriate behaviour at Stop TB** see *World Report* Lancet 2020; 396: 975

For more on the **Berlin Patient** see *Articles* Lancet 2020; 7: e340–47

For more on the **Berlin Patient** see *Obituary* Lancet 2020; 396: 1327

aking this law could be a 5-year jail
tence. In April, the supreme court
The Hague, Netherlands, approved
thanasia for patients with severe
mentia who have unbearable and
dless suffering, if they have provided
vritten request before they lose the
lity to express their will as a result
advanced dementia. This ruling
mes after a doctor was prosecuted
d acquitted for euthanising a woman
h severe Alzheimer's disease. In
tober, New Zealand voted to legalise
thanasia; this law is expected to
me into effect next November.
o of the criteria for assisted dying in
w Zealand will be a life expectancy
less than 6 months because of a
minal illness and the ability to make
informed decision.

## appropriate behaviour
## cusations

social media, former employees
de allegations against the global

suffers."

## Second HIV patient cured

On March 10, *The Lancet HIV* reported that a second patient had been cured of HIV after a CCR5Δ32/Δ32 allogeneic haematopoietic stem-cell transplantation. The London Patient, 40-year-old Adam Castillejo, was still in remission 30 months after analytical treatment interruption. Castillejo's HIV load in the plasma remained undetectable. Replication-competent HIV was also not detectable in the CSF, intestinal tissue, or lymphoid tissue.

Timothy Brown (the Berlin Patient) died on Sept 29, 2020, at the age of 54 years, after a recurrence of his leukaemia. Brown was the first person to be cured of HIV, in 2007, after receiving a stem-cell transplant when his leukaemia rebounded despite chemotherapy. He became an advocate of HIV cure research.

2020; 396: 876

For more on the **London Patient** see Articles *Lancet HIV* 2020; 7: e340–47

For more on the **Berlin Patient** see Obituary *Lancet* 2020; 396: 1327

Donneurs

Microbiote

GVH

LAM (MRD)

CAR-T

LAL

# COMPARAISON DES DONNEURS « ALTERNATIFS » et TRAITEMENTS PREVENTIFS DE LA GVHD

# DOUBLE USP vs HAPLO: the BMT CTN 1101 trial

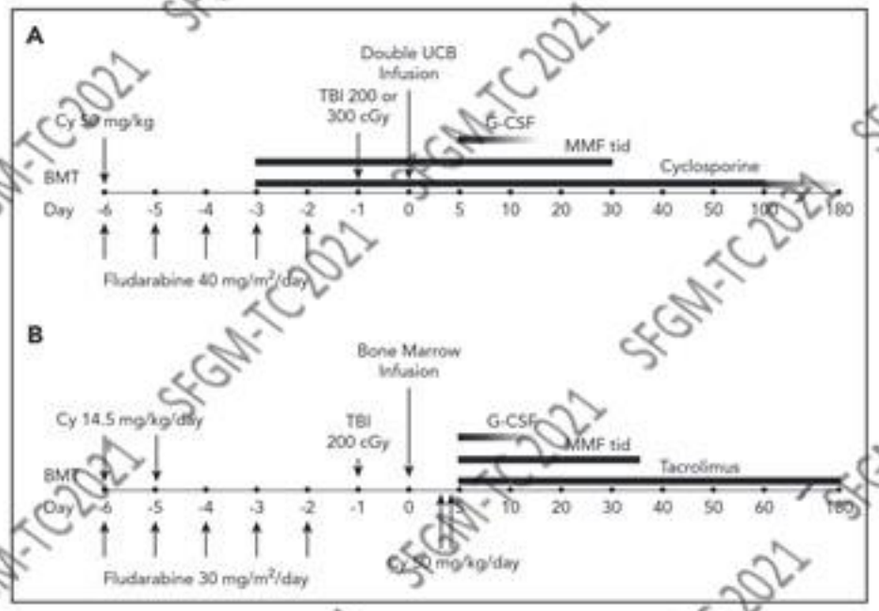
*Fuchs, Blood 2021*

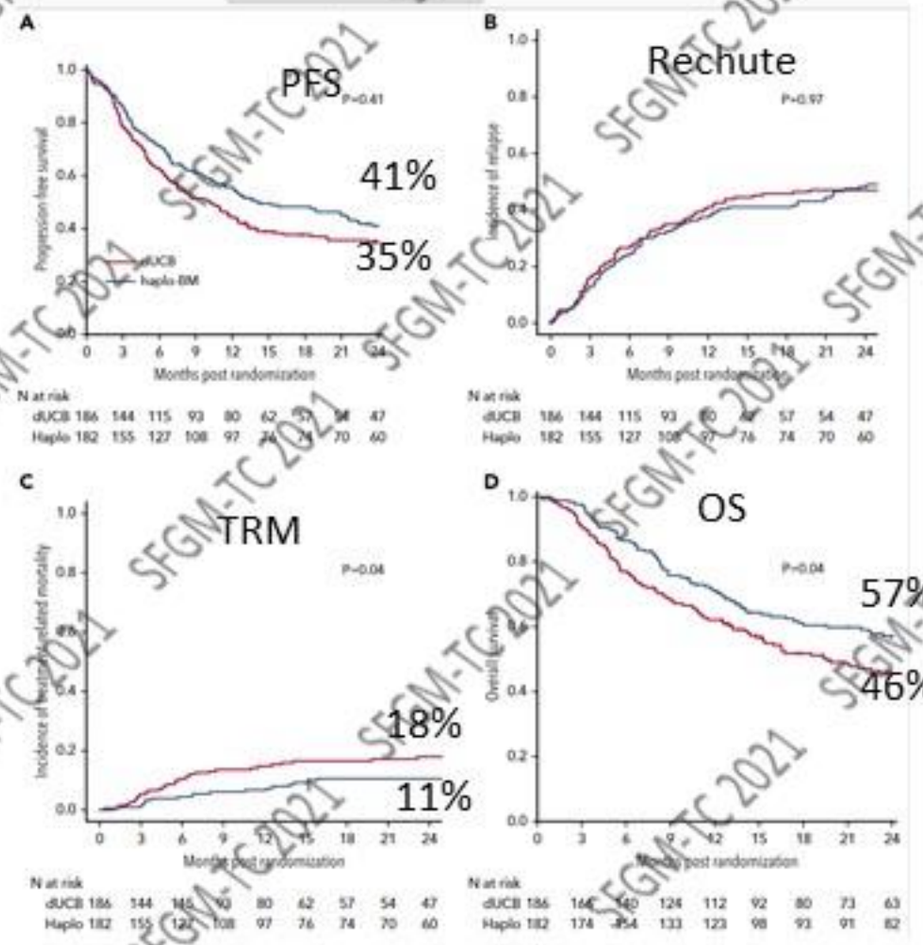
2 essais parallèles Lymphome ou LA en RC rando

**USP** (n=186)

**Haplo** (n=182)

CDT NMA




Taux important de rechute dans les 2

Haplo> USP car Moins de TRM

# HAPLO vs MUD avec PT-Cy

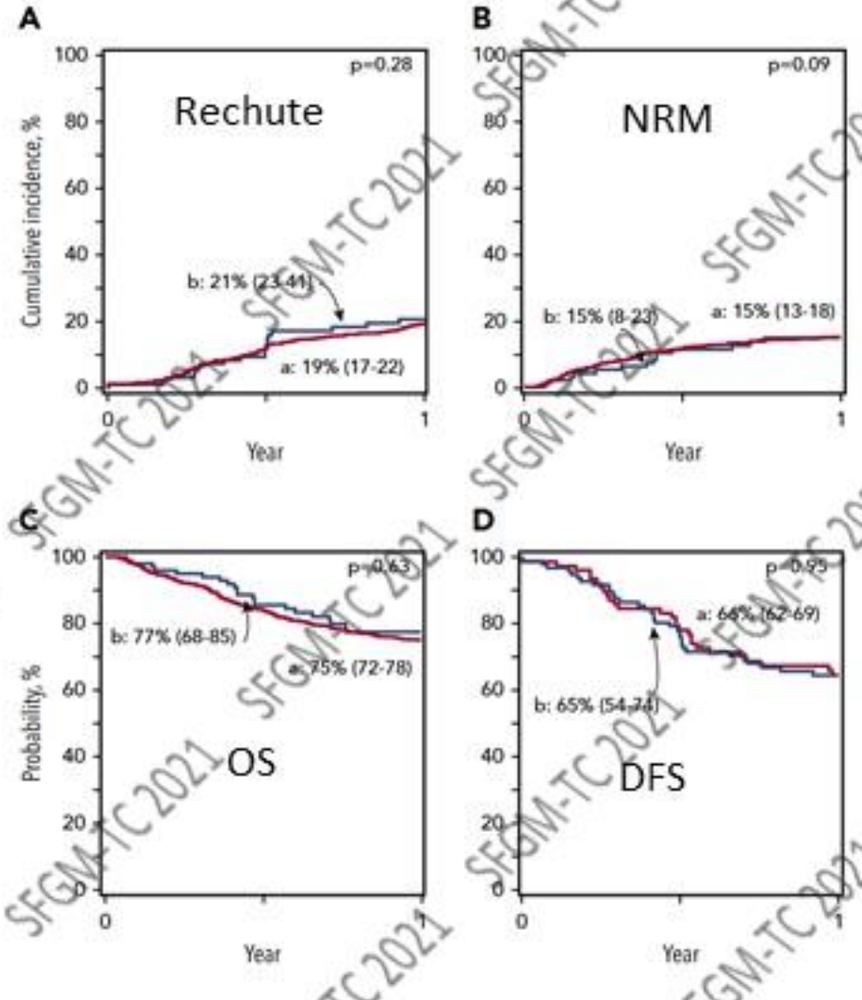
*M.Gooptu, Blood 2021*

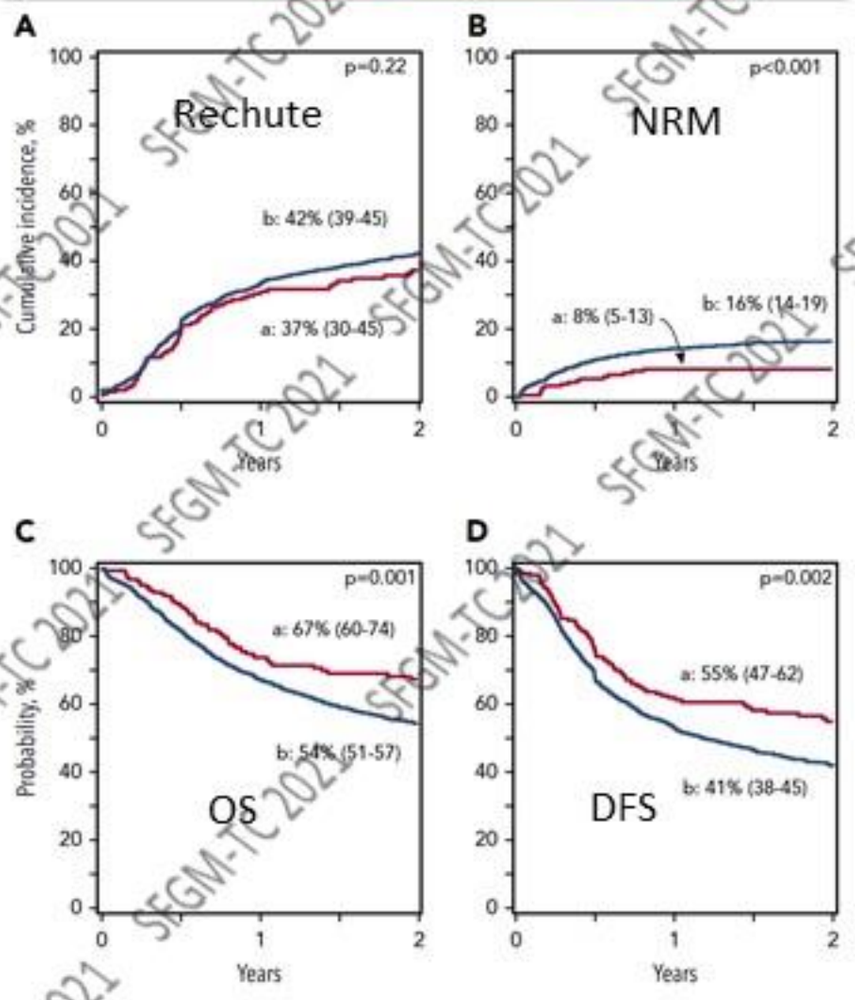
2036 Haplo vs 284 MUD avec Cy-PT, CNI, MMF
LA ou MDS adultes , DRI low/int
2011-2018 CIBMTR , 11 centres

MAC MUD-PT-Cy= Haplo-PT-Cy

RIC MUD-Cy PT > Haplo Cy-PT

| | MAC | RIC |
|---|---|---|
| **GVH 2-4** | | |
| Haplo | 37% | 33% |
| MUD | 33% | 27% |
| **GVH 3-4** | | |
| Haplo | 11% | 10% |
| MUD | 4% | 4% |
| **GVHc** | | |
| Haplo | 31% | 26% |
| MUD | 25% | 27% |



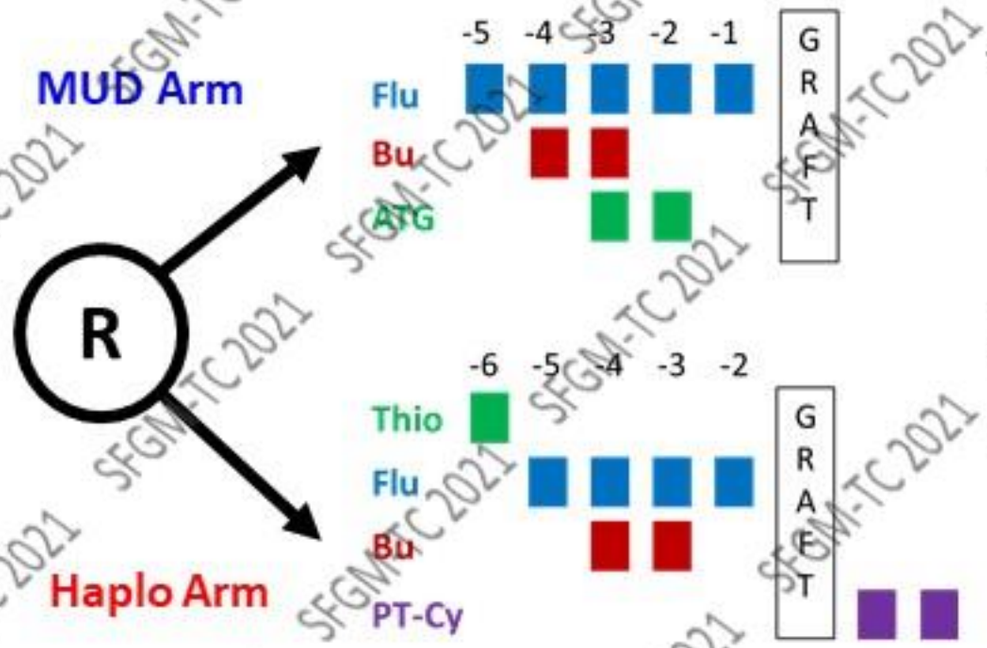
# Haplo PT-Cy vs. MUD ATG

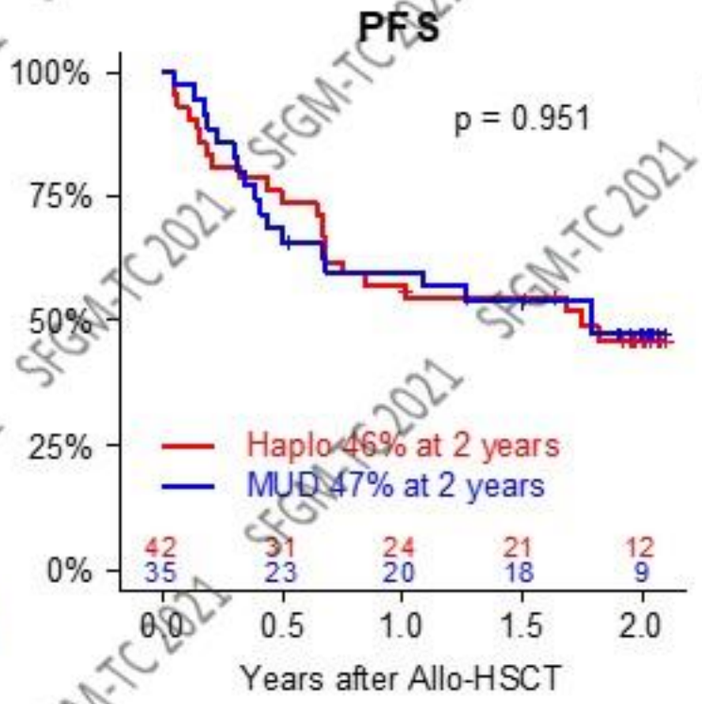
***HAPLOMUD-ELDERLY: NCT02623309***

PHRC-K

**N = 77**

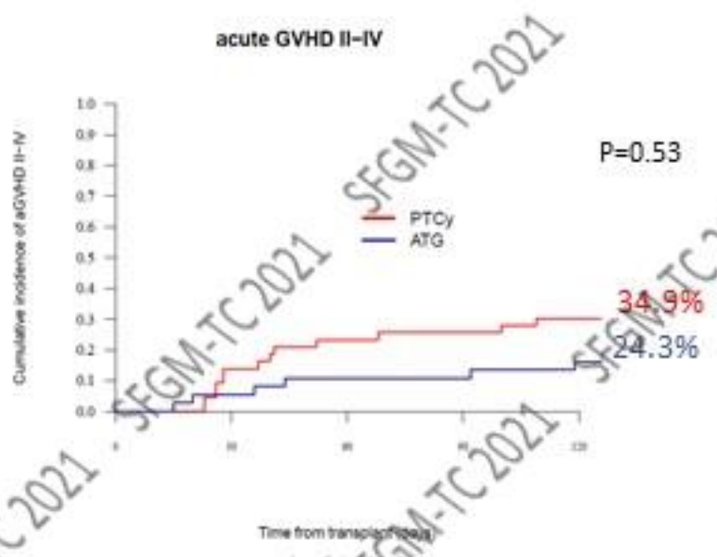
- Age: 55 to 70 years
- Hematological disease
- **No MSD available**

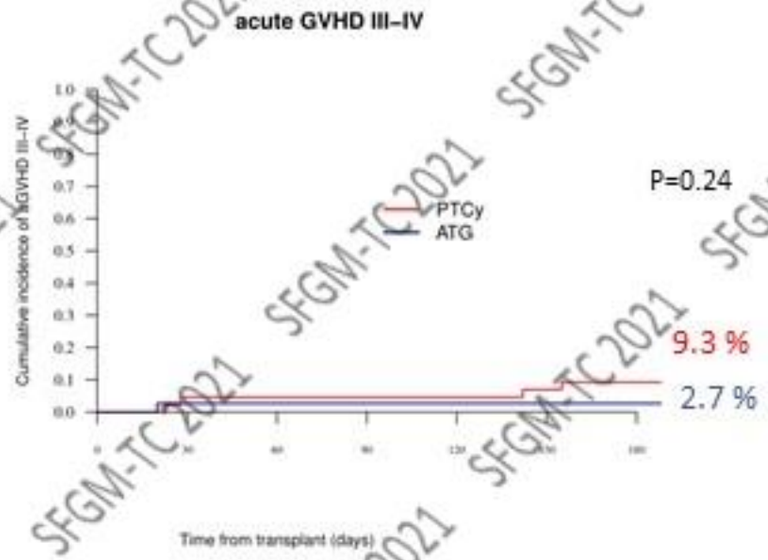


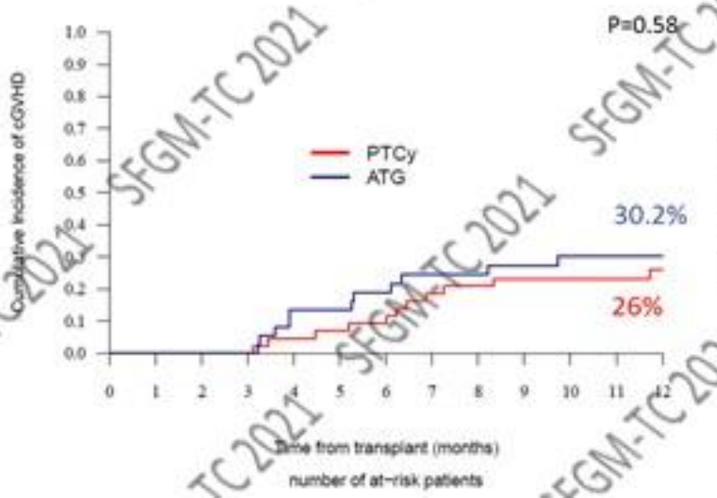

*Blaise in preparation*

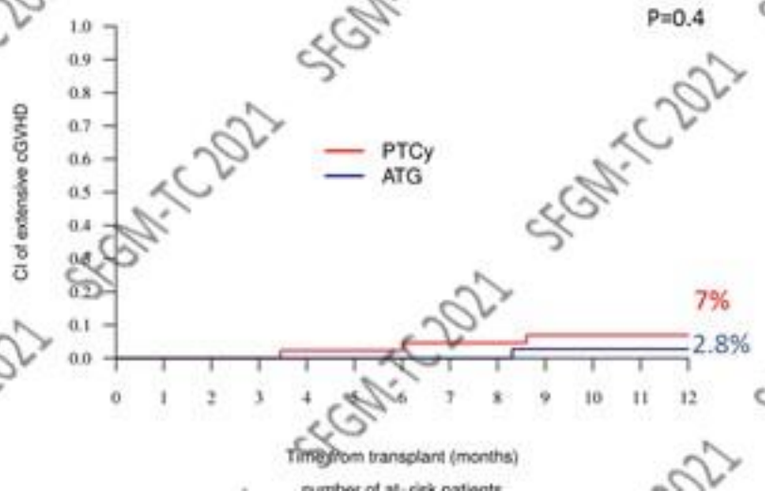
# PT-Cy vs ATG RIC 10/10; *E. Brissot et al EBMT 2021*




63-67% LAM/MDS
15% LNH
Âge médian 64 ans
MRD ou MUD 10/10



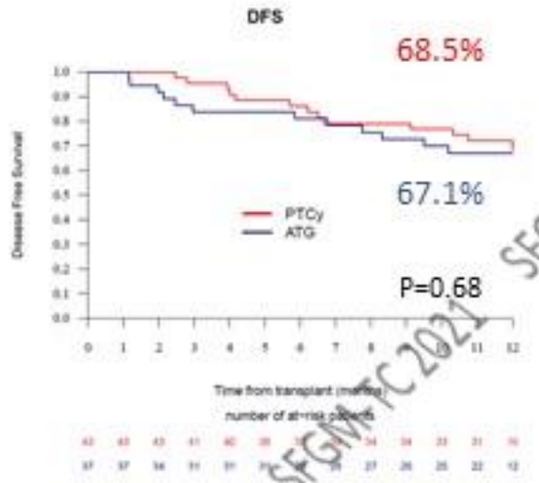



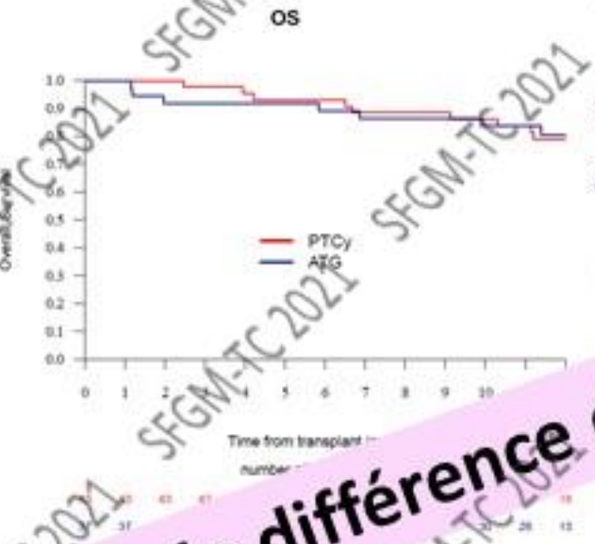

**FB2+ CSP**

43 **PT-Cy** 37 **ATG**

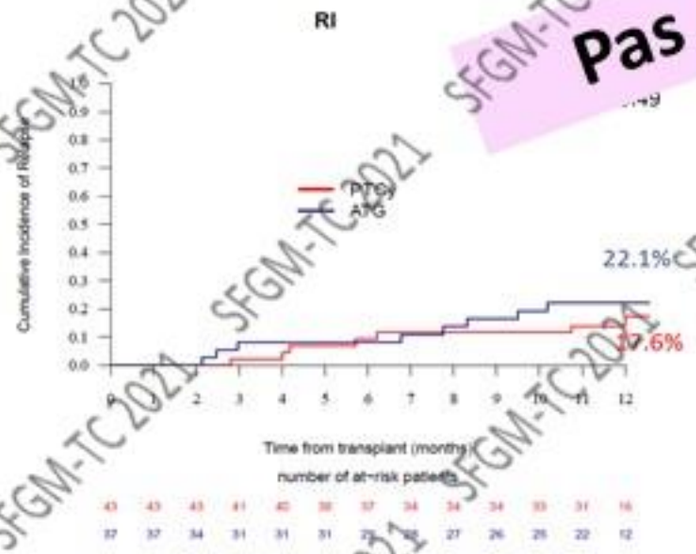
Ciclo +/- MMF (si MUD)

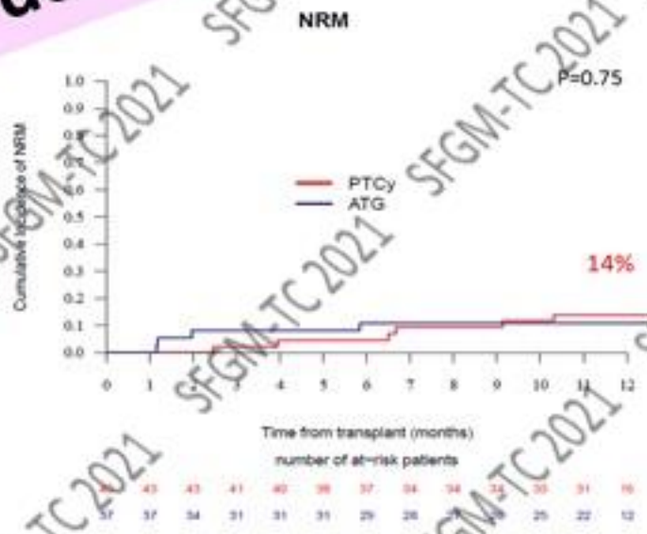
# PT-Cy vs ATG RIC 10/10; *E. Brissot et al*

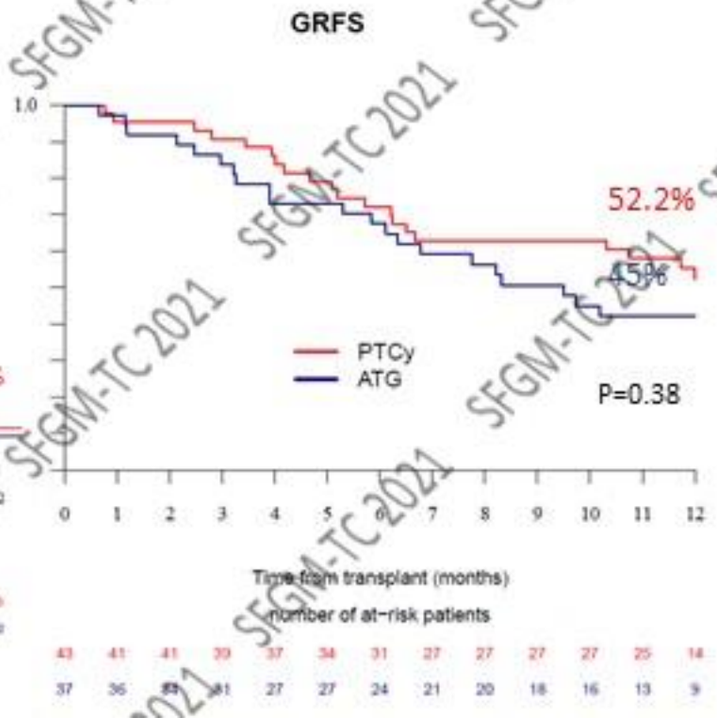



**Pas de différence entre PT-Cy et ATG**

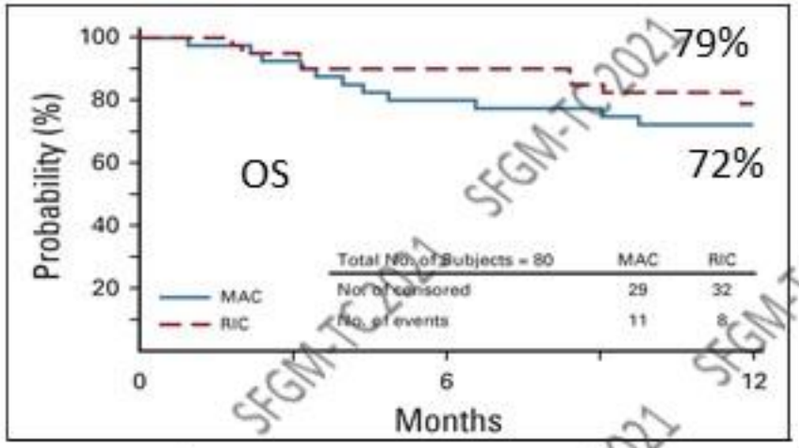


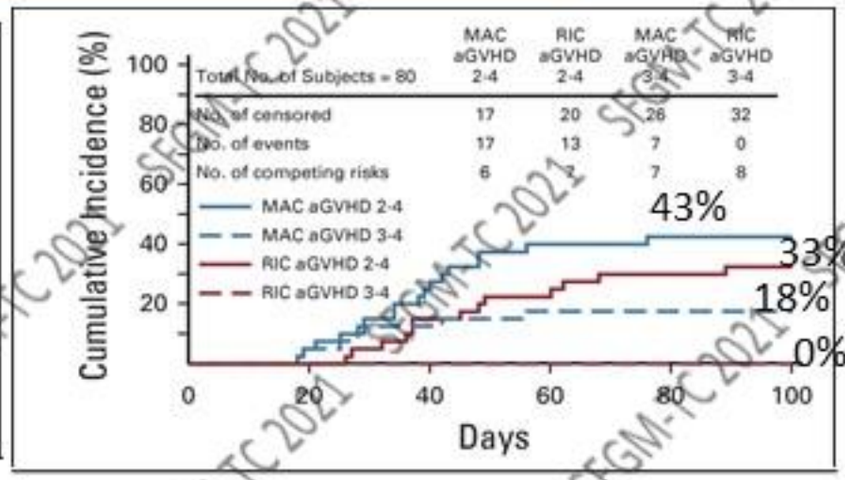



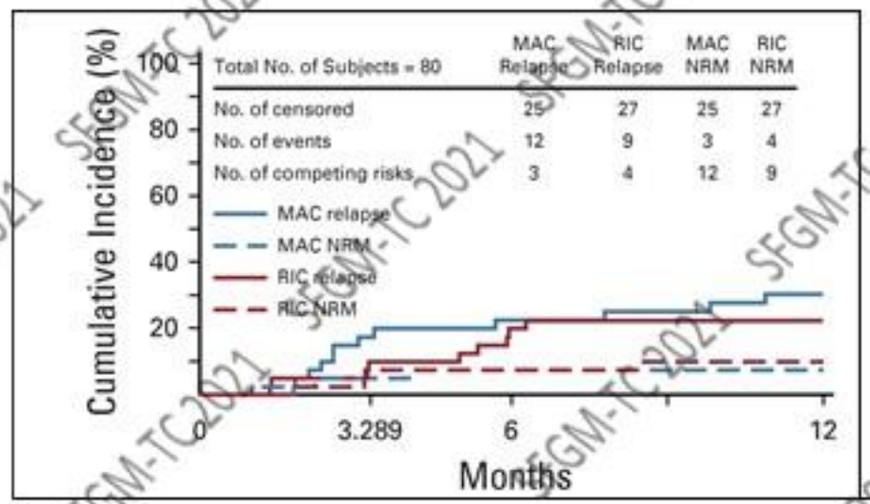



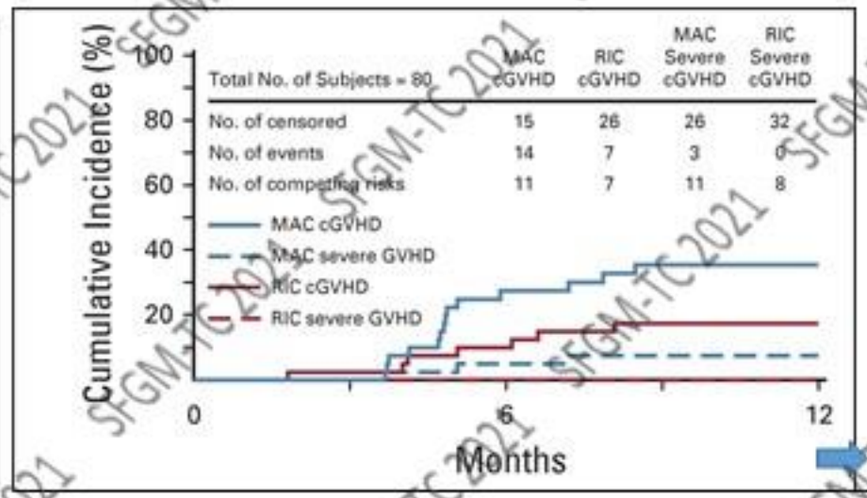
# PT-Cy dans les MMUD

*Bronwen E. Shaw, JCO 2021*




Phase 2 prospective Cy-PT MMUD (39% 4 à 6/8 match)
End point: OS 1 an>65%
N=80 pts dans 11 centres US, sponsor NMDP
LAM (46%), LAL (21%), LNH ou LH (20%)
51 ans med (18-70)

CDT MAC standart ou Bu Flu/ RIC: Baltimore

Greffon: moelle

PT-Cy J+3J+4
Sirolimus+ MMF J+5

48% minorités ethniques

GRFS 1 an: 38% MAC, 55% RIC

*Pour info, endpoint alter gref GRFS 2 ans 30% MMUD 9/10*

**Sirolimus prevention GVH MMUD,** Kornblit Blood 2021

N=77 MMUD NMA
Ciclo+MMF+SIROLIMUS

GVHD a 2-4 36% ; TRM18% ; Rechute et OS 62% à 4 ans

**Essai rando ATG dans les greffes MRD,** Chang JCO 2020

| | aGVHD 2-4 | GVHDc | GRFS 3ans |
|---|---|---|---|
| N=132 Ciclo MTX MMF+ATG 4.5 mg/kg | 13.7% | 28% | 38.7%; |
| N=131 Ciclo MTX MMF | 27% | 52% | 24.5%; |

**Abatacept (inh CTLA4) en prevention GVHa MUD** ;Watkins JCO 2021

| | | GVHa 3-4 | | Survie sans GVHa grave J+180 | |
|---|---|---|---|---|---|
| Rando double aveugle MUD 8/8 | CNI/MTX plus abatacept | 6.8% | *P* = .13 | 93.2% | *P* = .05 |
| | CNI/MTX plus placebo | 14.8% | | 82% | |
| Cohorte 7/8, non rando (contrôle matché) | CNI/MTX plus abatacept | 2.3% | *P* < .001 | 97.7% | *P* < .001 |
| | CNI/MTX | 30% | | 58.7% | |

## Dipeptidyl Peptidase 4 Inhibition for Prophylaxis of Acute Graft-versus-Host Disease

*Sherif S. Farag, M.D., Ph.D., N Engl J Med 2021*

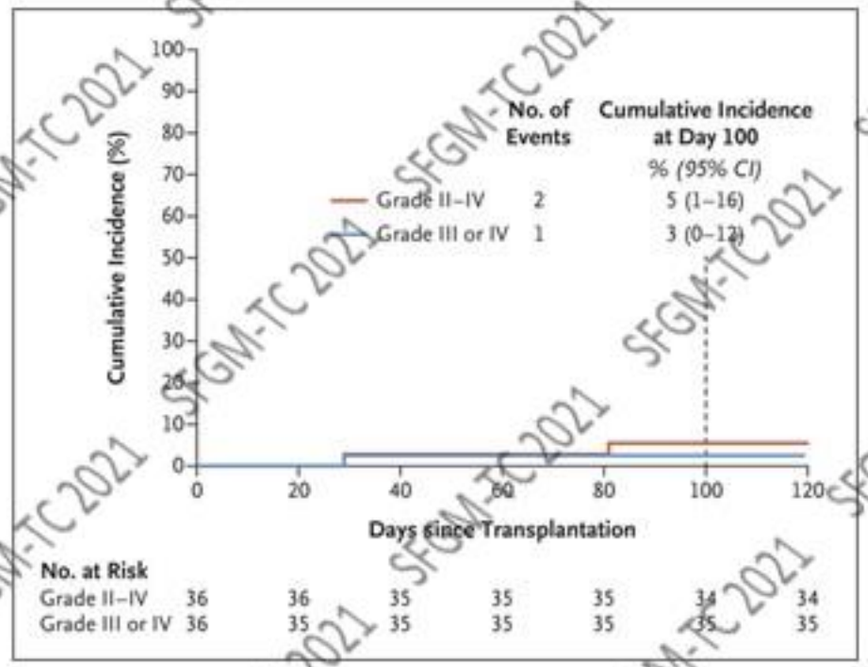
N=36 (med 46 ans) LAL, LAM, MDS, LMC ref ITK, MAC TBI 13Gy + EDX 120 ou Thiotepa 15mg/Kg + EDX 120

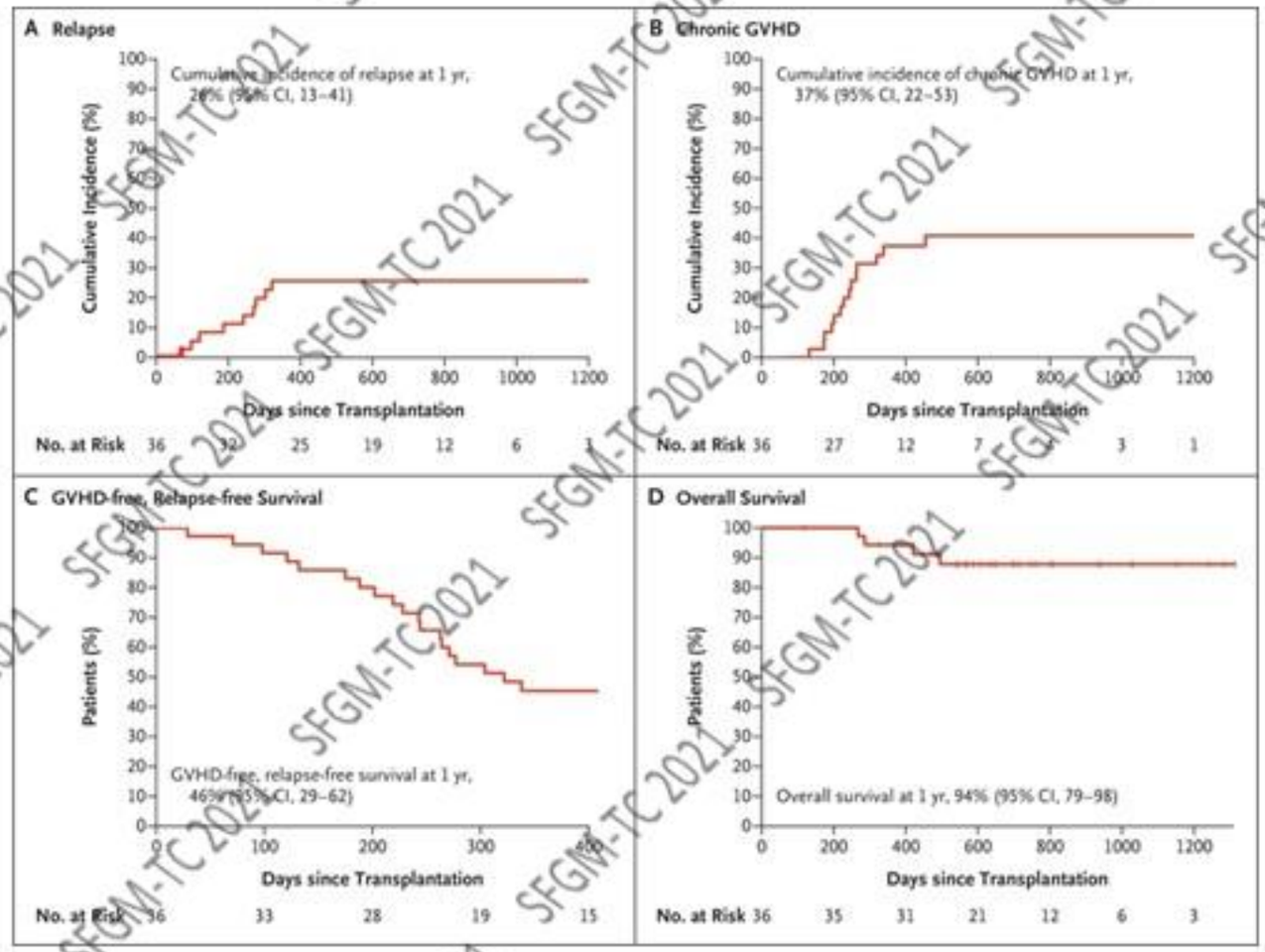
Prophylaxie GVH Tacro+ Sirolimus + **Sitagliptin: 600 mg x2 J-1 à J14**

Greffon CSP, MRD ou MUD

Pour info: Januvia dose diabète: 100mg/j

NRM 1 an= 0%!



# Effet du Sitaglipin sur la GVH?

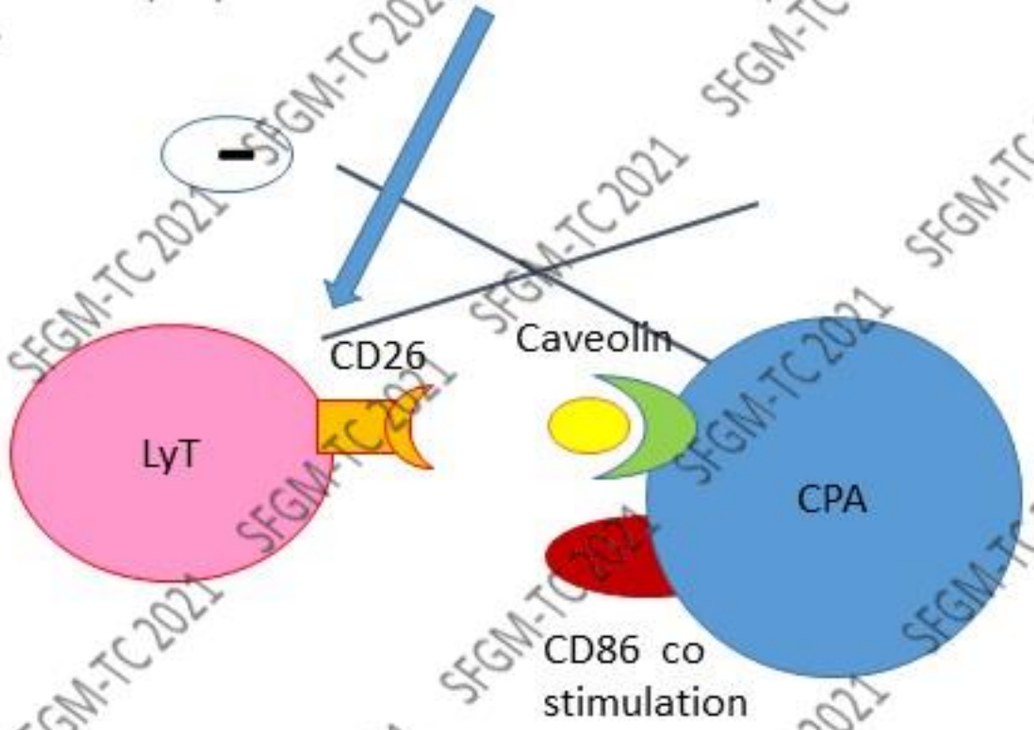
Sitagliptin inhibe l'activité dipeptidyl peptidase 4 (DPP-4) du CD26, exprimé à la surface de beaucoup de cellules

**DIABETE**

Sitaglipin — DPP4

Dégrade les hormones stimulant insuline

Favorise P°endogène insuline



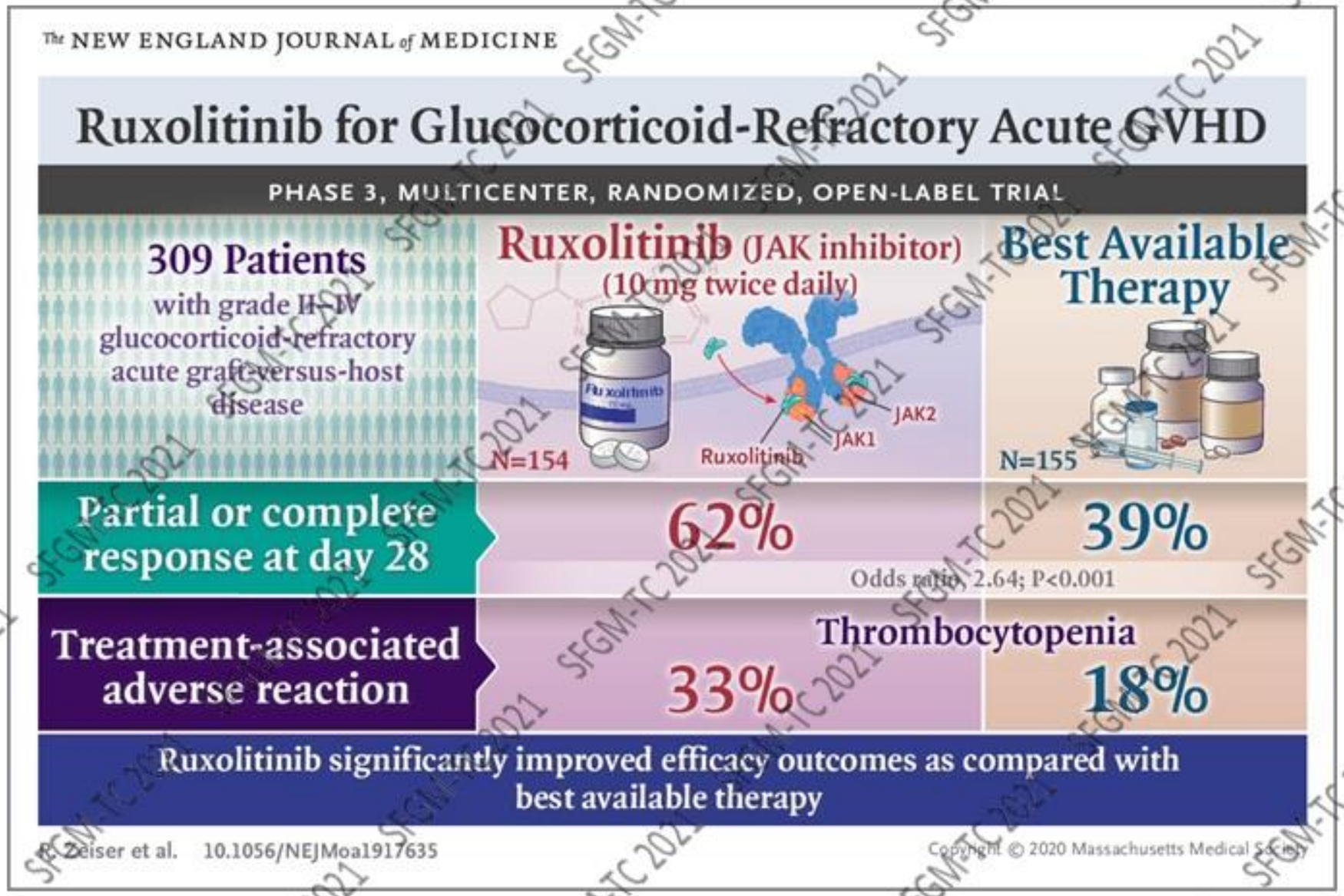

**Greffes USP**

Empêche la dégradation defacteurs de croissance P° cellules hémato dans la moelle (SDF1/CD34)

On attend l'étude randomisée!

# TRAITEMENTS CURATIFS DES GVHD CORTICO RESISTANTES

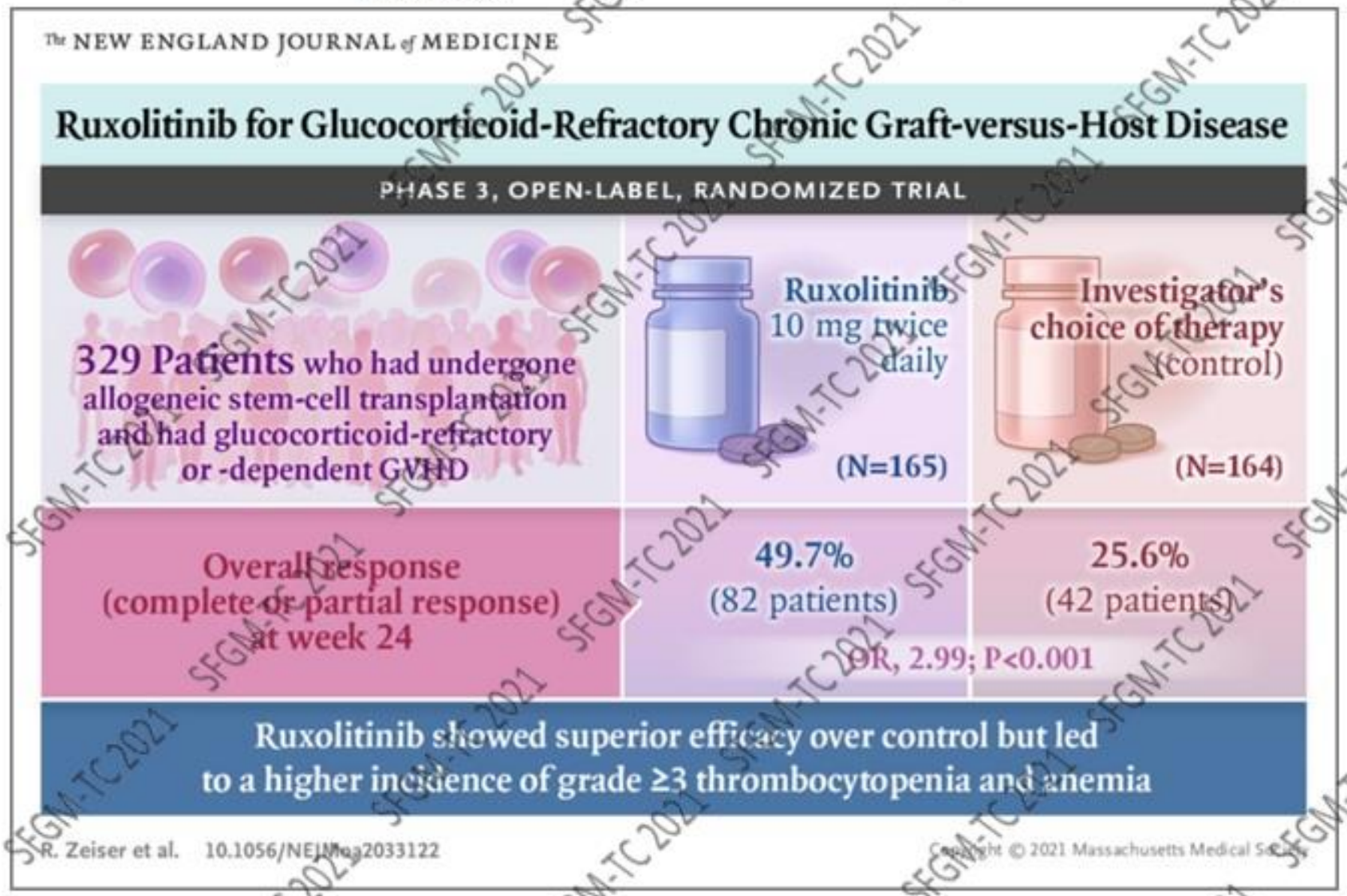
REACH-2




The estimated cumulative incidence of loss of response at 6 months was 10% in the ruxolitinib group and 39% in the control group. The median failure-free survival was considerably longer with ruxolitinib than with control (5.6 months vs. 1.0 month; hazard ratio for relapse or progression of hematologic disease, non–relapse-related death, or addition of new systemic therapy for acute GVHD, 0.46; 95% CI, 0.35 to 0.60). The median overall

# Ruxolitinib for Glucocorticoid-Refractory Chronic Graft-versus-Host Disease

July 15, 2021
N Engl J Med 2021




Ruxolitinib led to longer median failure-free survival than control (>18.6 months vs. 5.7 months; hazard ratio, 0.37; P<0.001) and higher symptom response (24.2% vs. 11.0%; odds ratio, 2.62; P=0.001).

**JAK1 (IFN, Herpes)**

**Itacitinib**

GRAVITAS-301:phase 3 rando

Abstract EHA 2020. Zeiser R. 295076; S256

439 pts

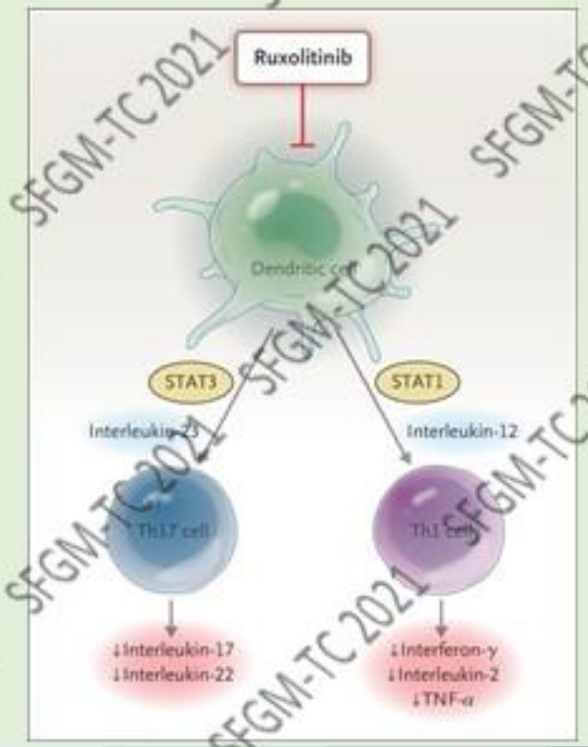
ITA + CS, n=219 PBO + CS, n=220)

Pas de différence

Day 28 ORR, 6-mo NRM, or OS

**JAK1 et 2 (cytopénies)**

**Ruxolutinib**




**JAK1 et 3 (IMS)**

**Tofacitinib**

PAR

Granulomatoses

**Filgotinib**

Colite ulcérée; Feagan B., Lancet 2021

**Baricitinib**

Efficacy and Safety of Baricitinib in Refractory Chronic Graft-Versus-Host Disease (cGVHD): Preliminary Analysis Results of a Phase 1/2 Study

Noa G. Holtzman, ASH 2020

**ROCK2 Inhibition With Belumosudil (KD025) for the Treatment of Chronic Graft-Versus-Host Disease**

Madan Jagasia; JCO 2021

The rho-associated coiled-coil–containing protein kinase-2 (ROCK2) signaling pathway regulates the Th17/regulatory T cells balance and controls profibrotic pathways.

Selective ROCK2 inhibition with belumosudil (KD025)

A phase IIa, belumosudil doses 200mg ou 400mg/j

RESULTS

N=54 pts cGVHD ≥ 3 lines

median follow-up of 29 months

**ORR 62% à 69%**

a median duration of response of 35 weeks

CS treatment was discontinued in 19% of patients.

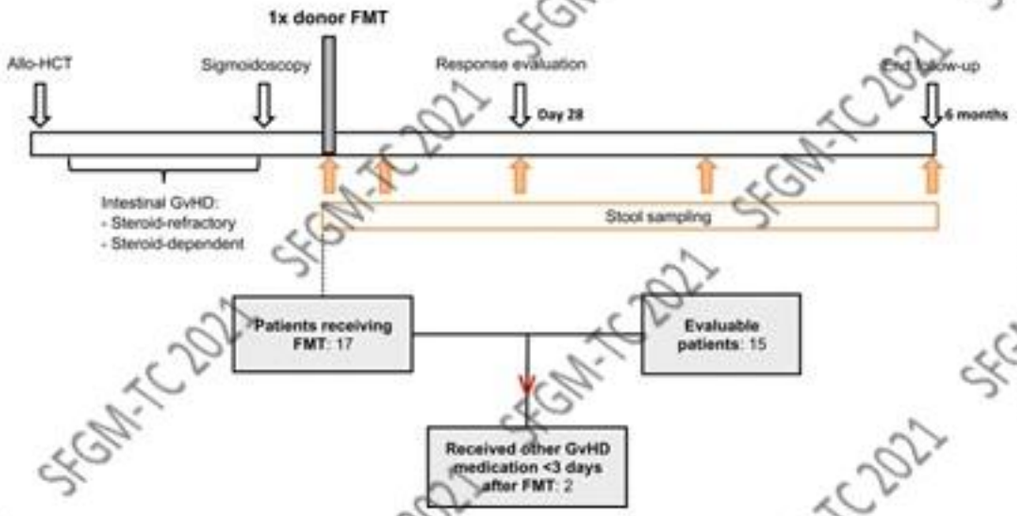
The failure-free survival rate was 76% and 47% at 6 and 12 months

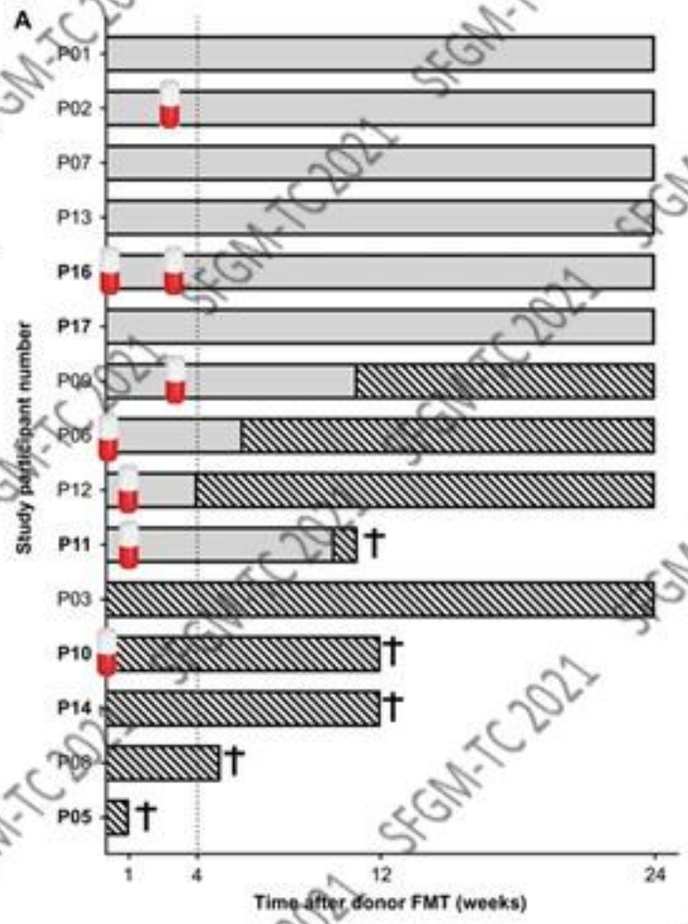
The 2-year OS 82%

Safe

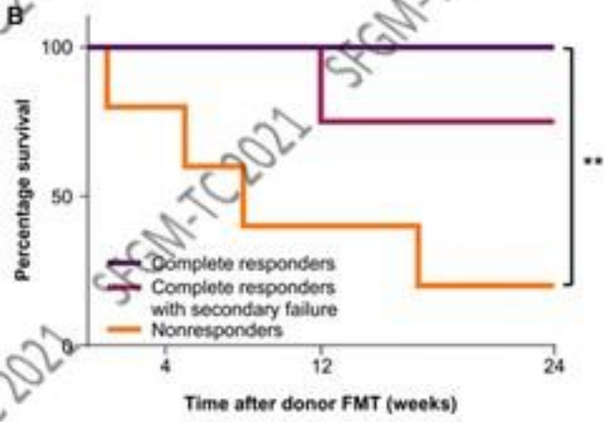
**Donor fecal microbiota transplantation ameliorates intestinal graft-versus-host disease in allogeneic hematopoietic cell transplant recipients**

*Sci Transl Med 2020, Van Lier Y.*



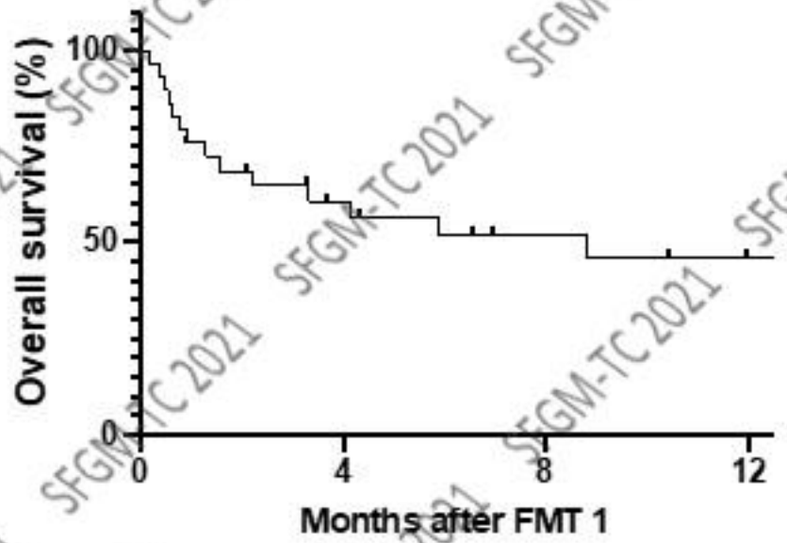

10 RC /15 dont 6 avec arrêt IMS




- Amélioration diversité microbiote
- Tp partielle du microbiote donneur
- Augmentationbacteries productrices butyrate (clostridia et Blautia)

# FMT for SR GI aGVHD: results of French CUP

- N=29 steroid-resistant GI-aGVHD (resistance n=22, dependance n=7)
  - classical aGVHD n=22, late-onset aGVHD n=2; aGvHD with overlap syndrome n=5
  - Median 3 previous line of treatment (range, 1-5), 22 patients received ruxolitinib
- MaaT013 biotherapeutic (pool of donors)
- FMT 1-3 enema (median: 3)
- At day 28: ORR 59%, CR 31%
- 12 months OS: 46% (median FU 313 days)



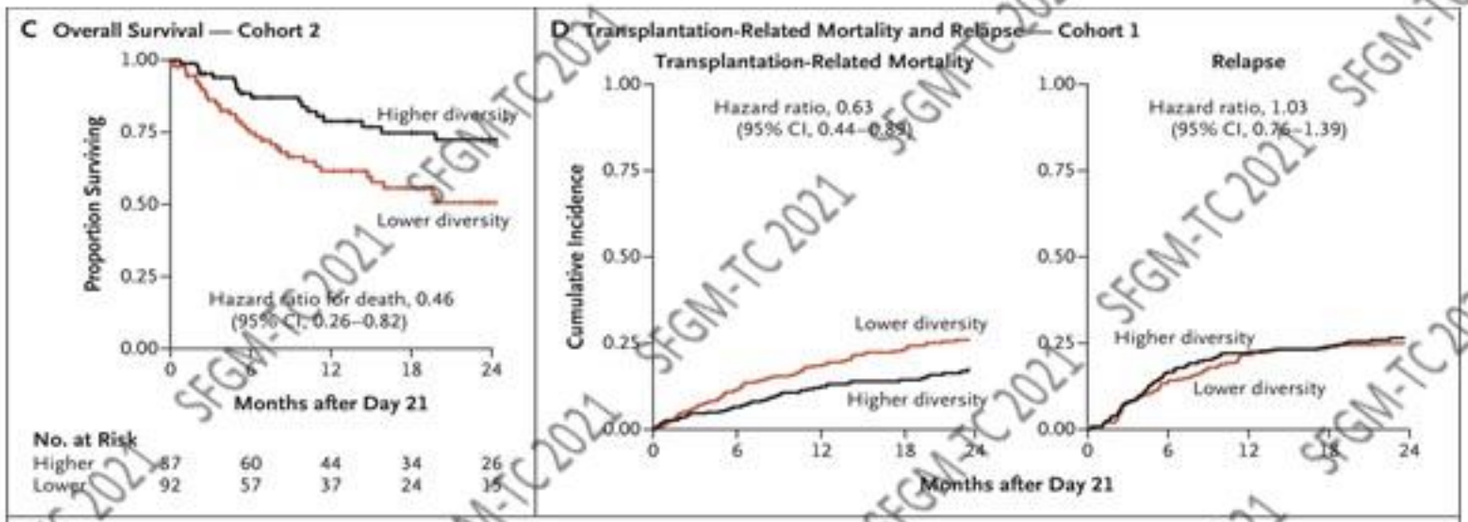

- Safety: one possibly related sepsis, resolutive with antibiotic

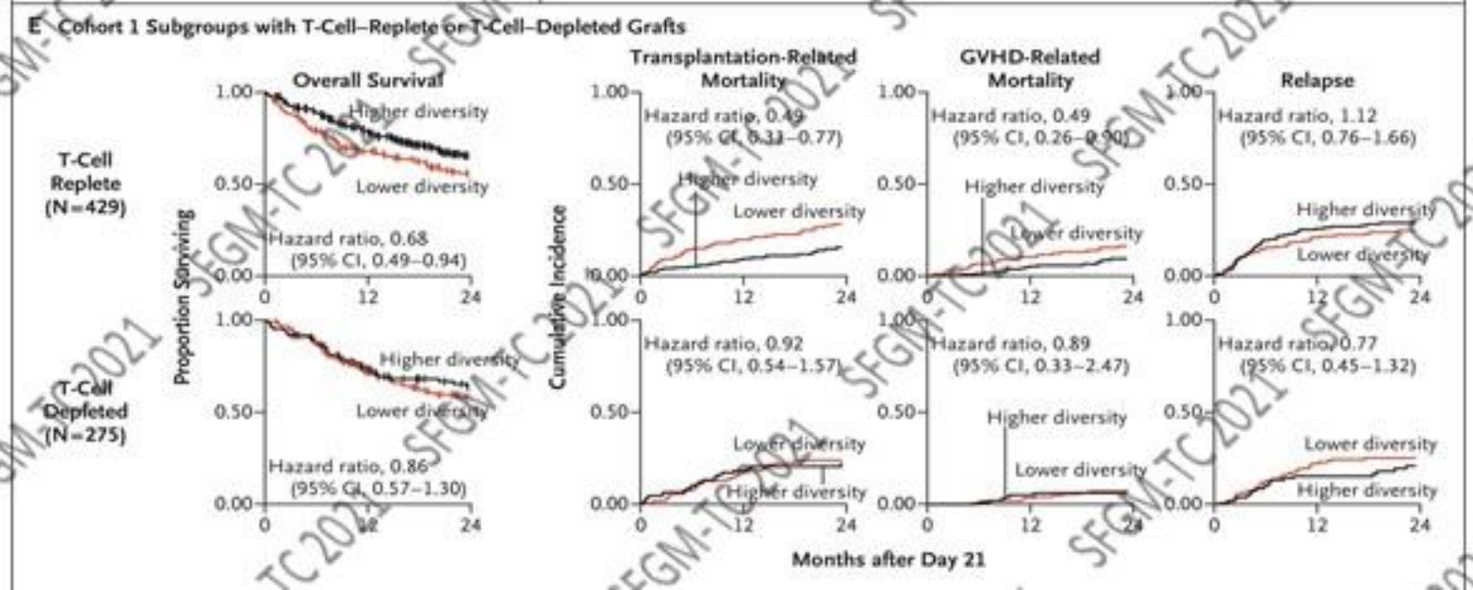
*Malard et al., EBMT 2021 oral session*

# MICROBIOTE

# Microbiota as Predictor of Mortality in Allogeneic Hematopoietic-Cell Transplantation

Jonathan U Peled, NEJM 2020




8767 selles de 1362 allo dans 4 centres(New York, Allemagne, Japon, Caroline Nord)

Pré TP et post-Tp J7-J21

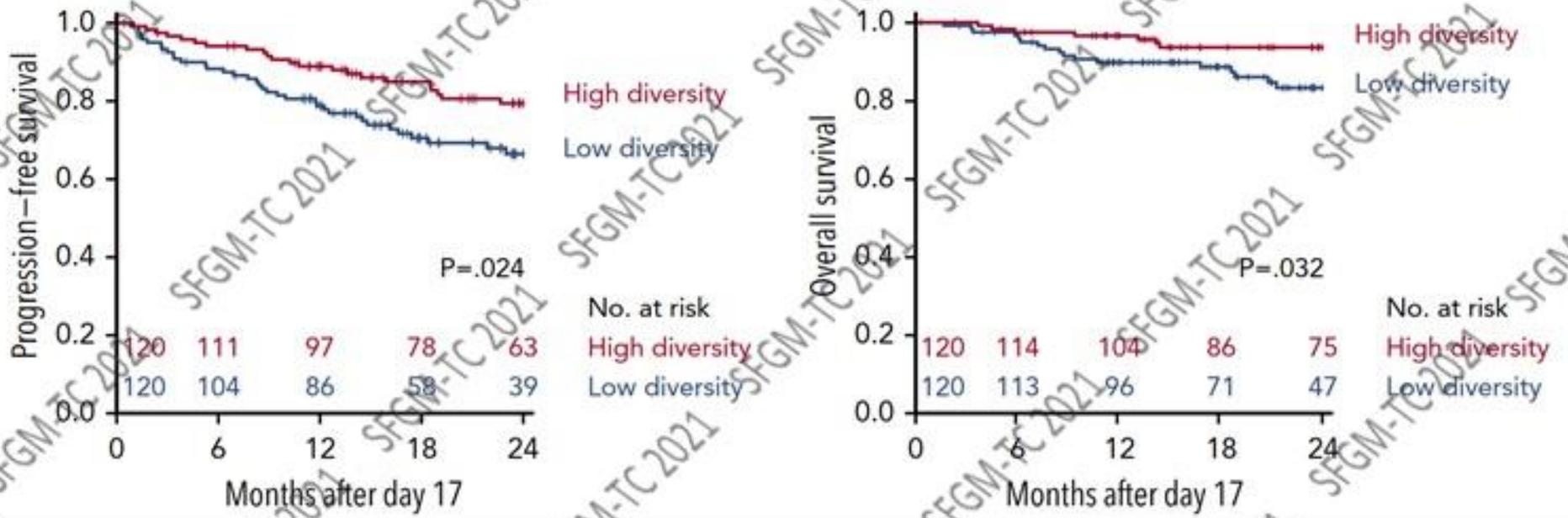
## Fecal microbiota diversity disruption and clinical outcomes after auto-HCT

*Niloufer Khan, Blood 2021*

1161 fecal samples collected from 534 adult recipients of auto-HCT for lymphoma, myeloma, and amyloidosis in an observational study conducted at 2 transplantation centers in the United States. By using 16S ribosomal gene sequencing

**D**

Patients with an available peri-engraftment stool sample



# LAM/MDS

# Impact of Conditioning Intensity of Allogeneic Transplantation for Acute Myeloid Leukemia With Genomic Evidence of Residual Disease

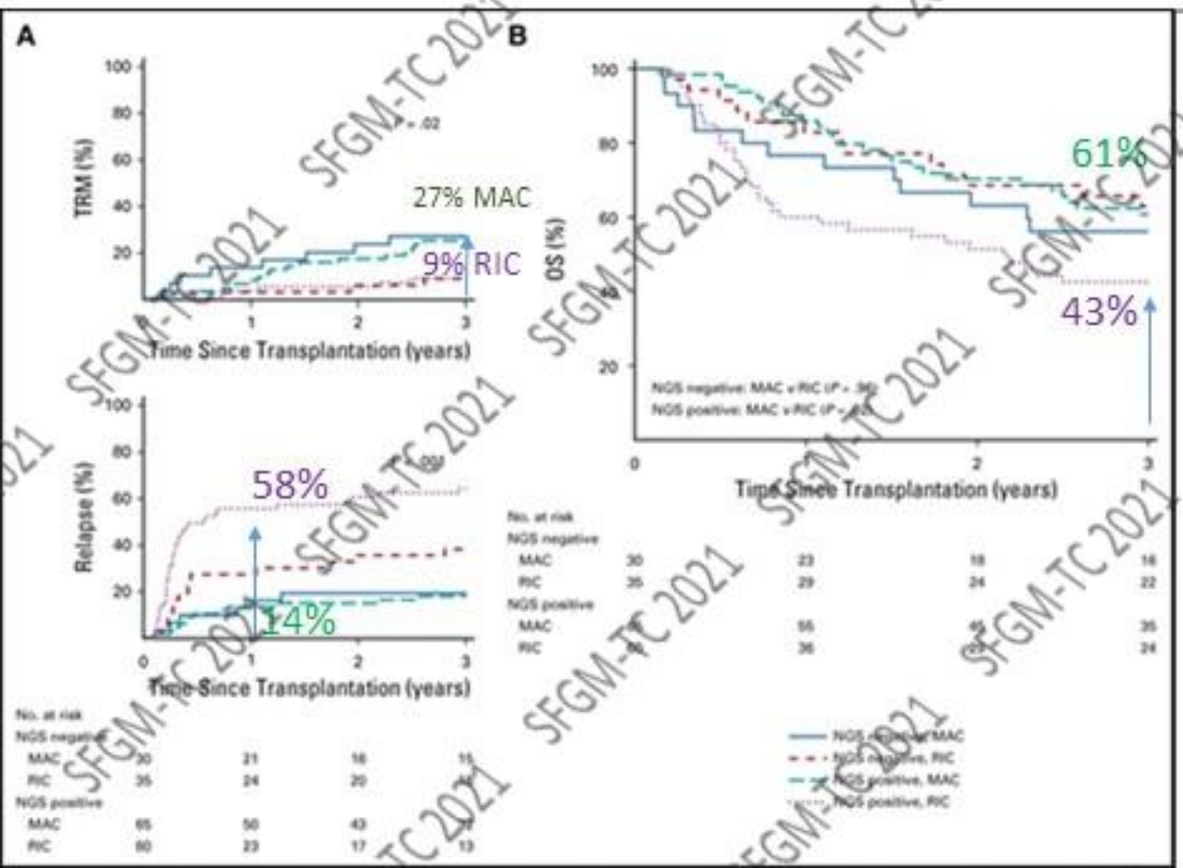
*Christopher S. Hourigan, JCO 2020*

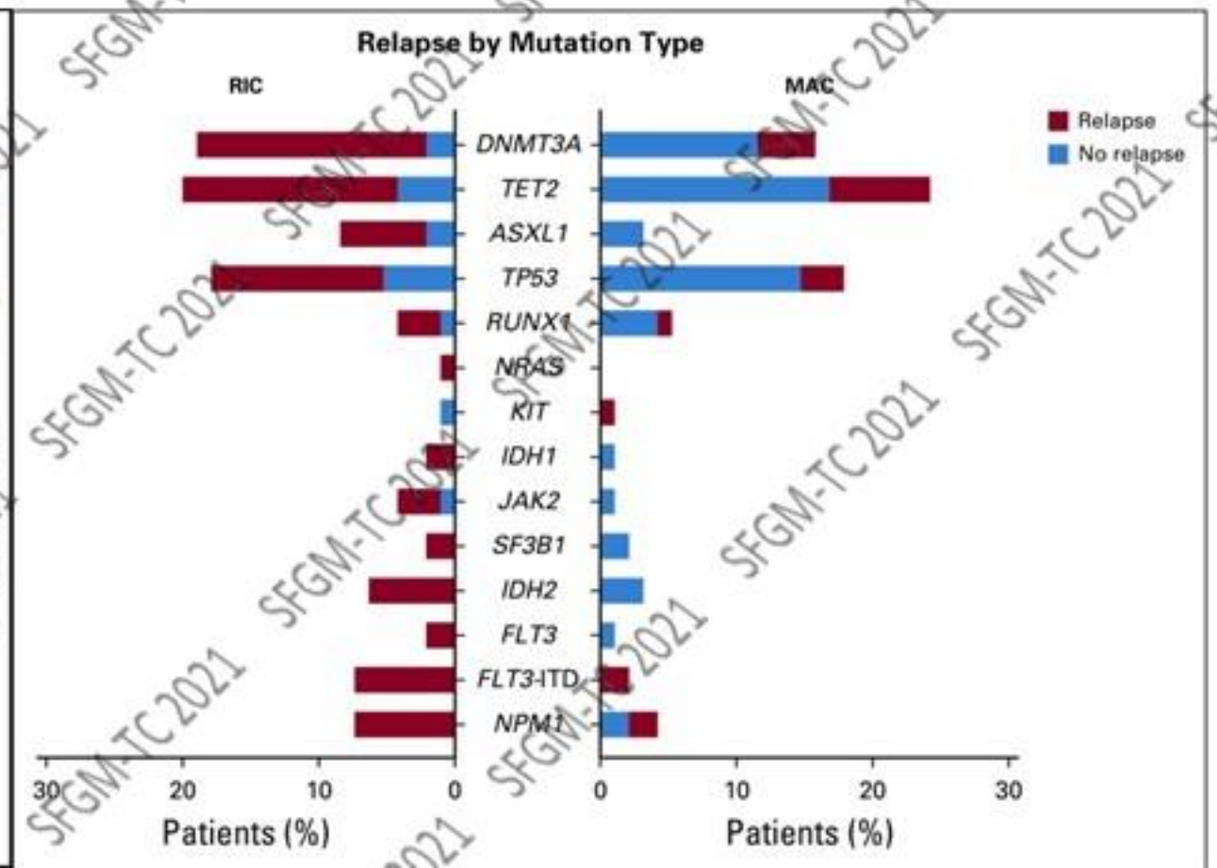
N=190 LAM 55 ans (22-66), en RC1 cyto
NGS 13 gènes en pré greffe

BMT-CTN 0901 study

N=95 RIC

N=95 MAC



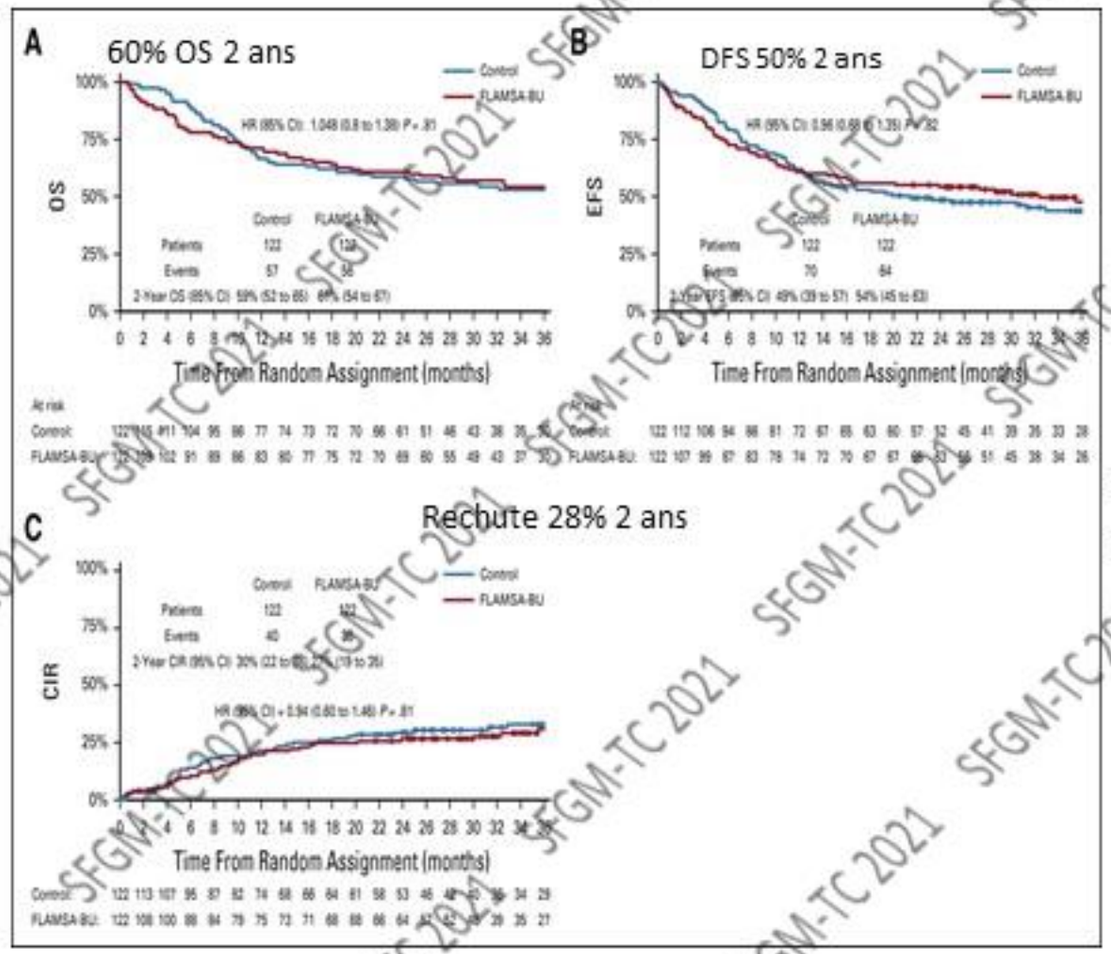



**Augmented Reduced-Intensity Regimen Does Not Improve Postallogeneic Transplant Outcomes in Acute Myeloid Leukemia**
*Craddock, étude FIGARO: JCO 2021*

N=244 rando LAM/MDS ht risk
Med 59 ans (22-75)

→ N=108 RIC

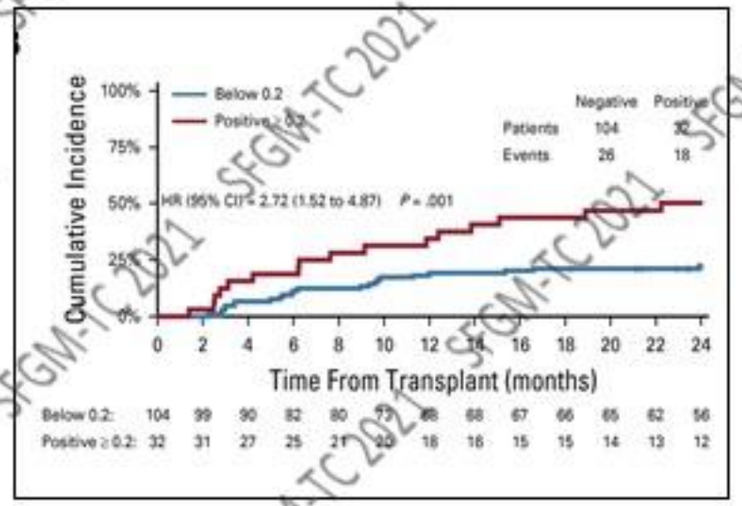
→ N=108 FLAMSA-Bu




Pas de différence
RIC vs Flamsa Bu

**Impact délétère de la MRD cytométrie pré greffe sur les rechutes et OS**

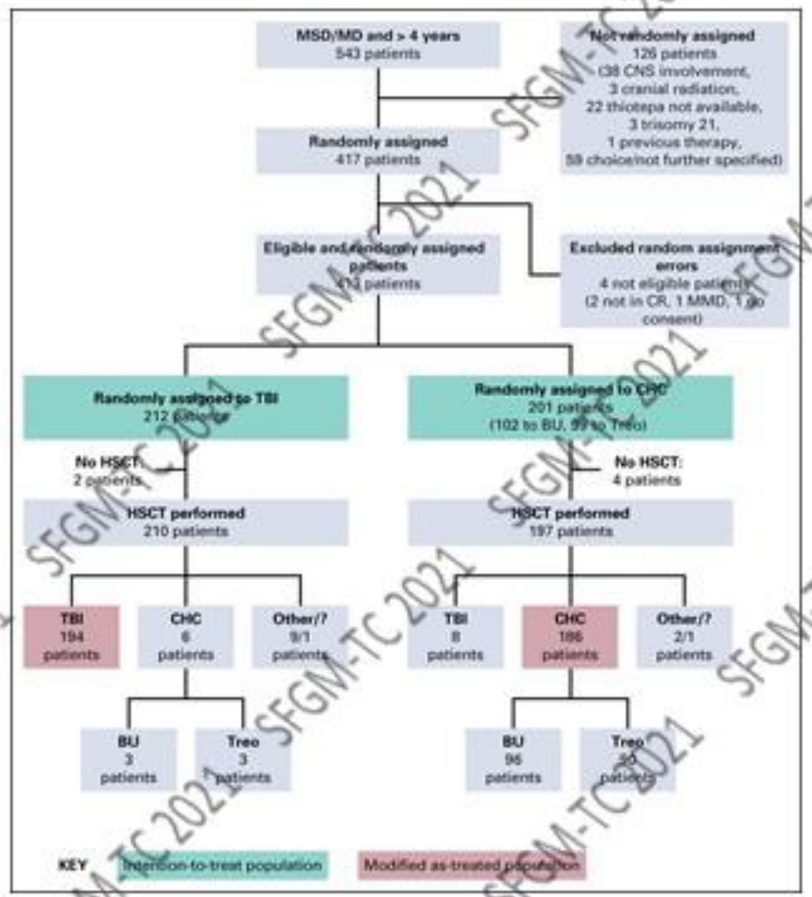
CIR à 2 ans: 20% si MRD <0.2% vs 50% si MRD >0.2%
OS 2 ans : 68% vs 50%

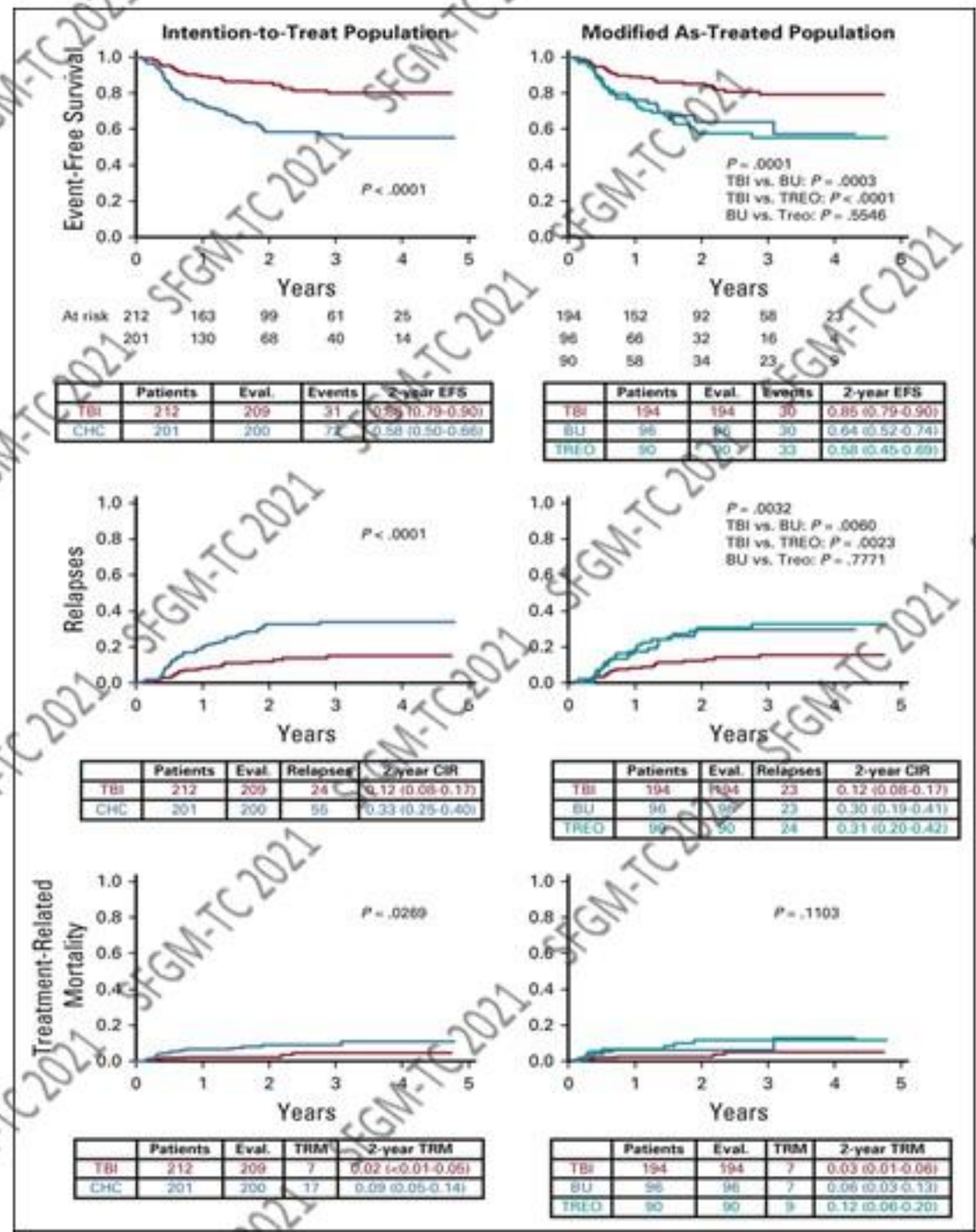


LAL

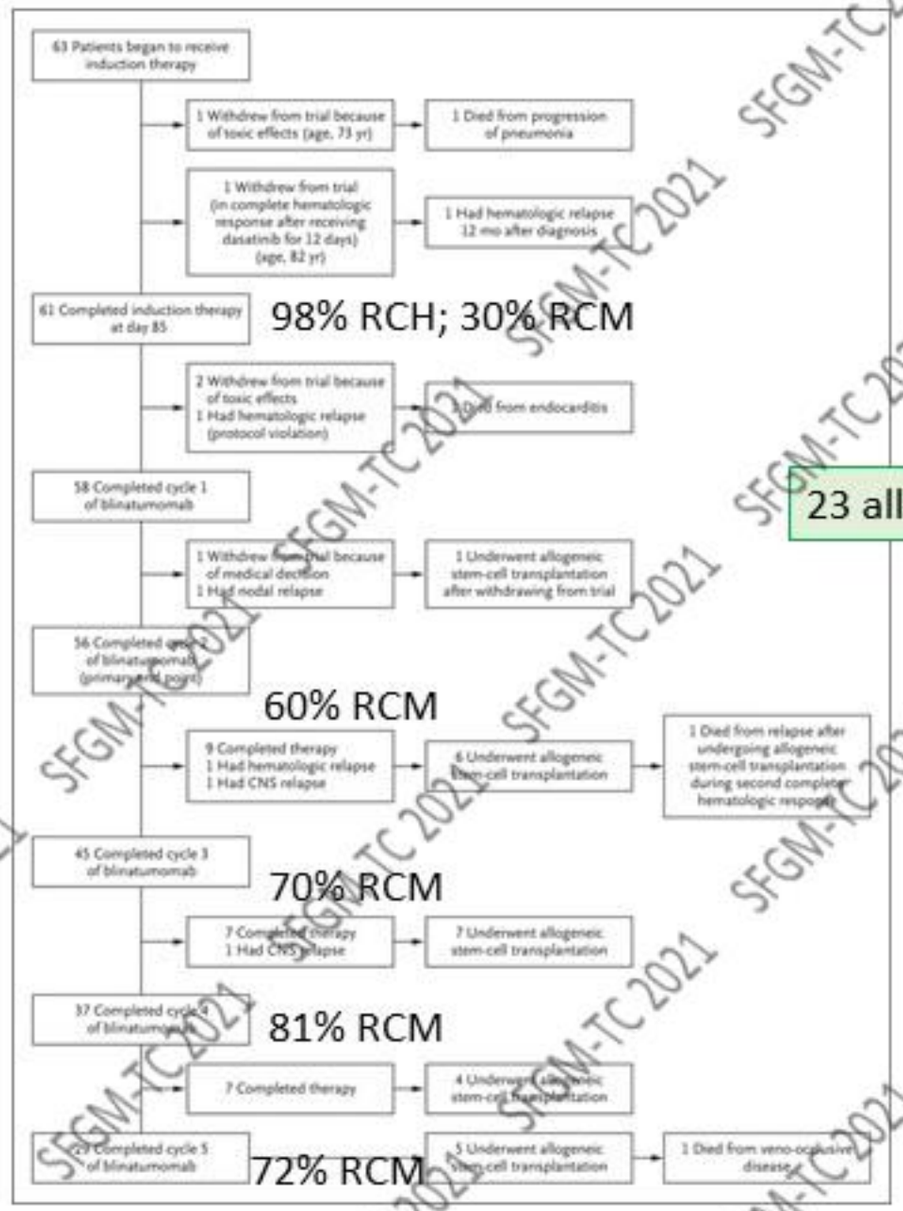
# Total Body Irradiation or Chemotherapy Conditioning in Childhood ALL: A Multinational, Randomized, Noninferiority Phase III Study; *C. Peters JCO 2021*

FORUM



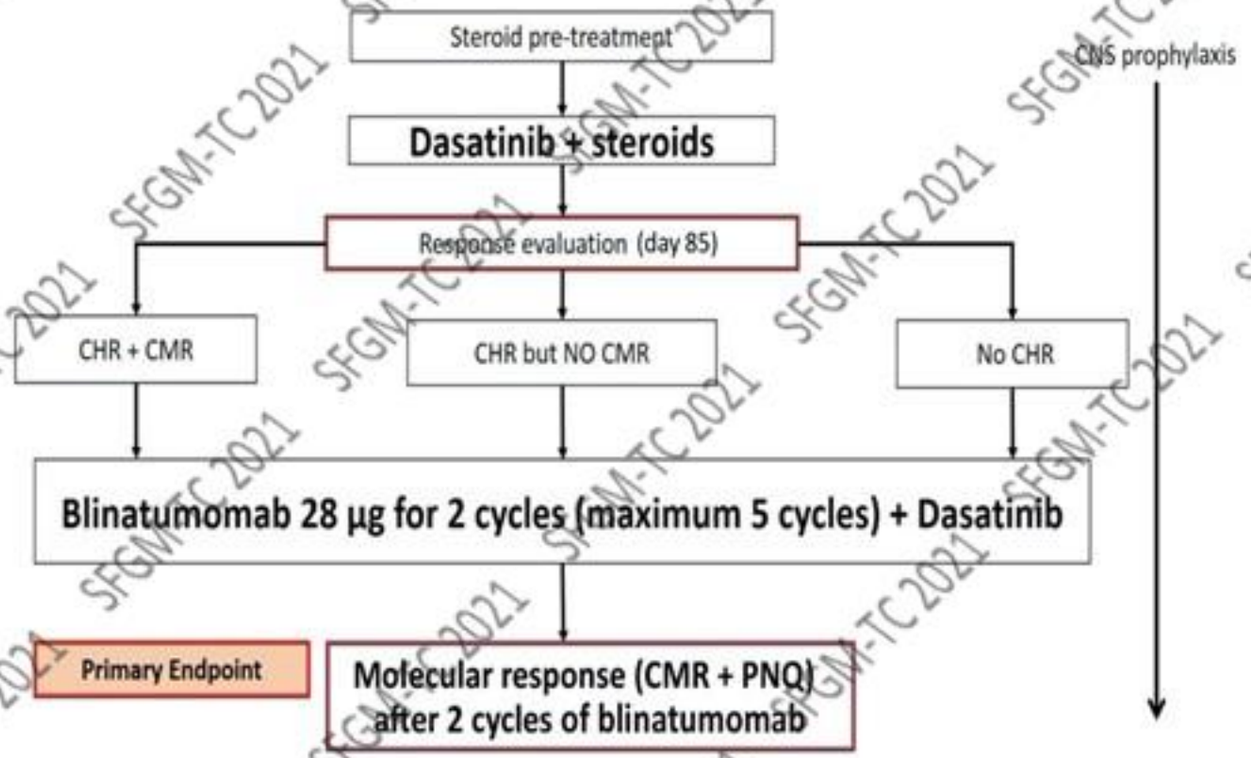
N=63 ALL Phi+ 54 ans (24-82)

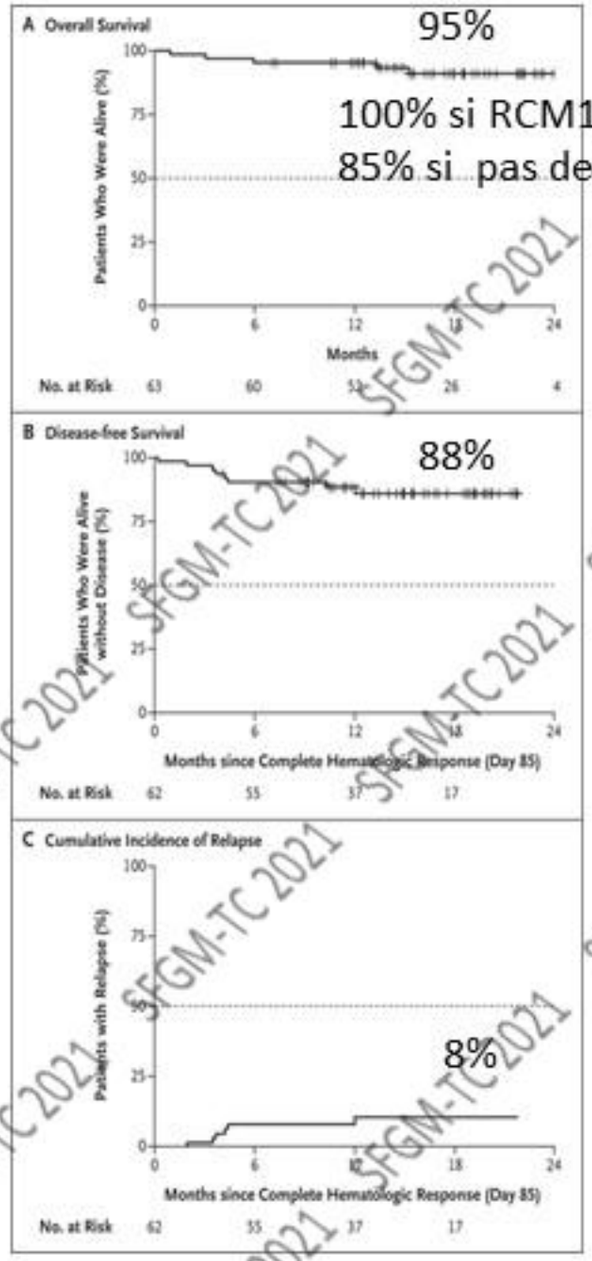


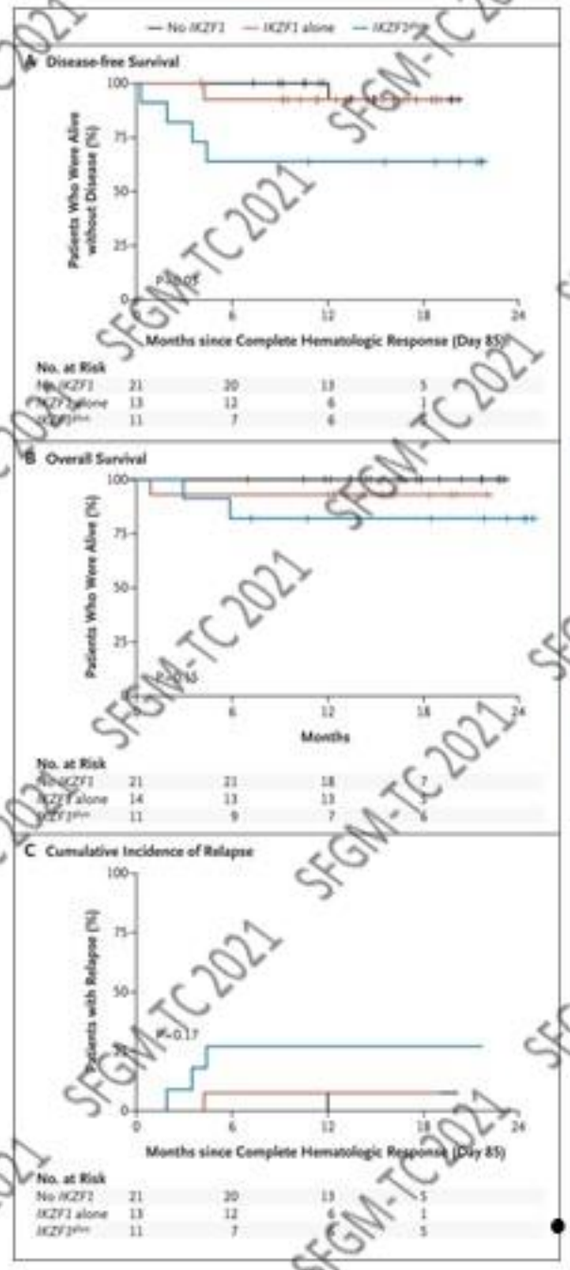

23 allo

**Dasatinib–Blinatumomab for Ph-Positive Acute Lymphoblast**
**Leukemia in Adults**

Robin Foà, M.D., N Engl J Med 2020






**N=23 allo en RC1/63**

17/23 (74%) MRD1+
6/23 (26%) RCM
Après 2 Blina: 11/23 (48%) MRD +
2 DC (8%) , TRM 4%

**Place de l'allo dans cette stratégie chemo-free?**
**En fonction de la MRD?**
**De la del Ikaros?**
**De la survenue de mutation?**

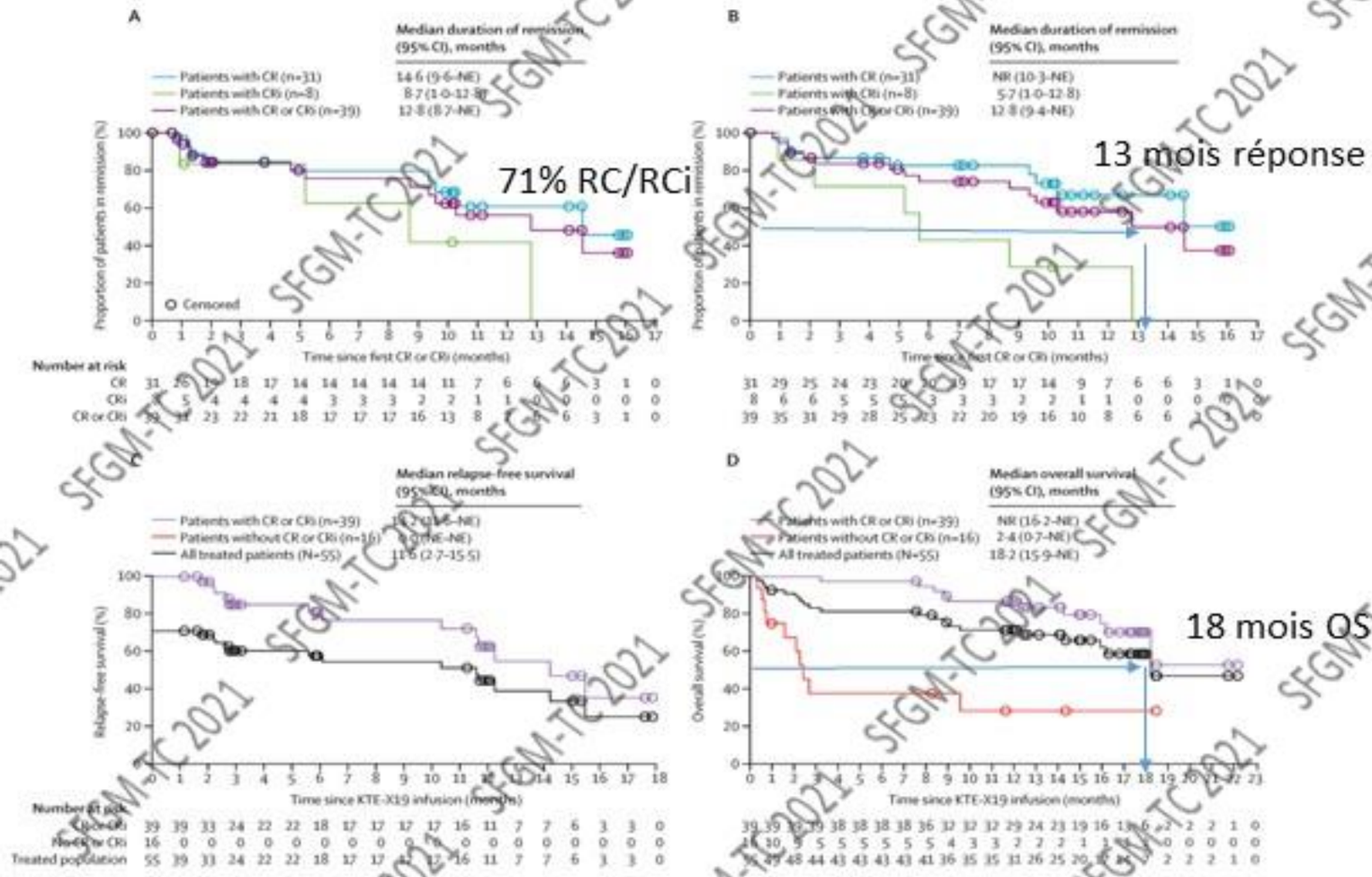
Med follow up 18 mois

*Robin Foà, M.D., N Engl J Med 2020*

**KTE-X19 for relapsed or refractory adult B-cell acute lymphoblastic leukaemia: phase 2 results of the single-arm, open-label, multicentre ZUMA-3 study**

B.Shah, Lancet 2021

N=71 inclus >5% blastes MO → 55 injectés 1x106/Kg CART-CD19/CD28




71% RC/RCi

13 mois réponse

18 mois OS

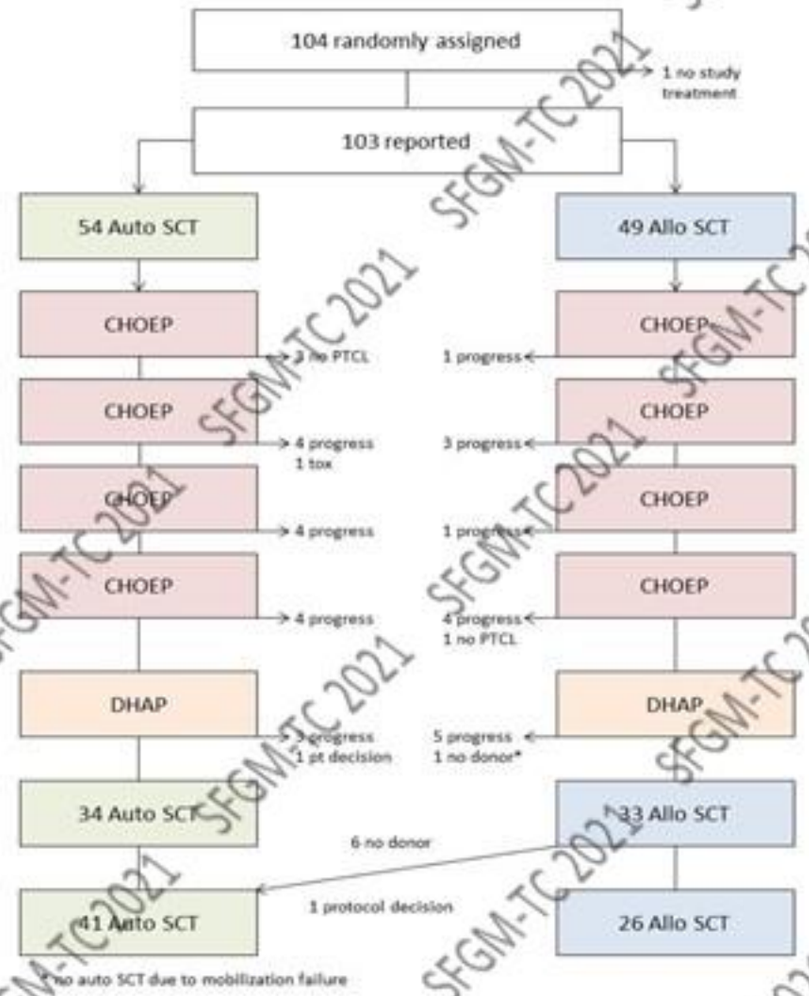
71% RC/Rci dont 97% en MRD neg
2 DC liés KTE (cerebral, choc septique)
Expansion corrélée réponse
Persistance non corrélée réponse
18% allo (n=10), pas d'effet sur la durée de réponse

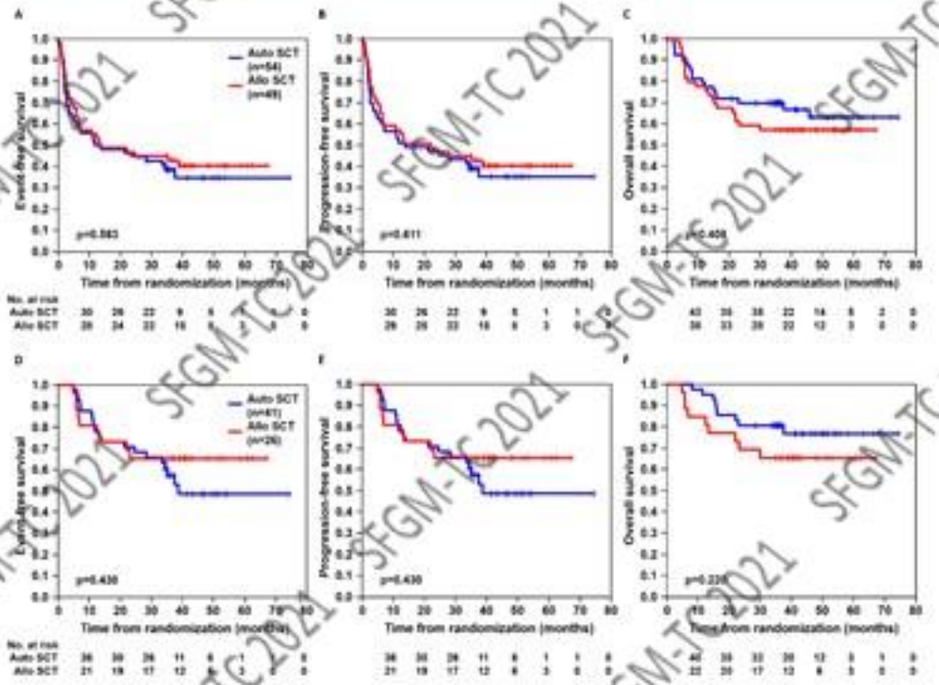
| | KTE Zuma3 | Blina Tower | Inotuzumab Inovate |
|---|---|---|---|
| OS | 18mo | <8mo | <8mo |
| Durée Reponse | 13mo | 7.3 rep | 4.6mo |

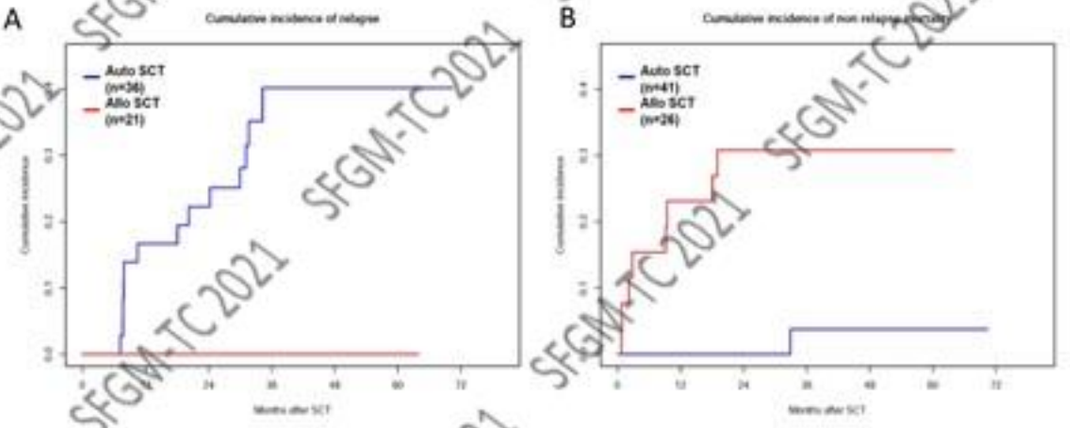
LNHT

# A randomized phase 3 trial of autologous vs allogeneic transplantation in first-line therapy in poor-risk peripheral T-NHL

Norbert Schmitz, Blood 2021



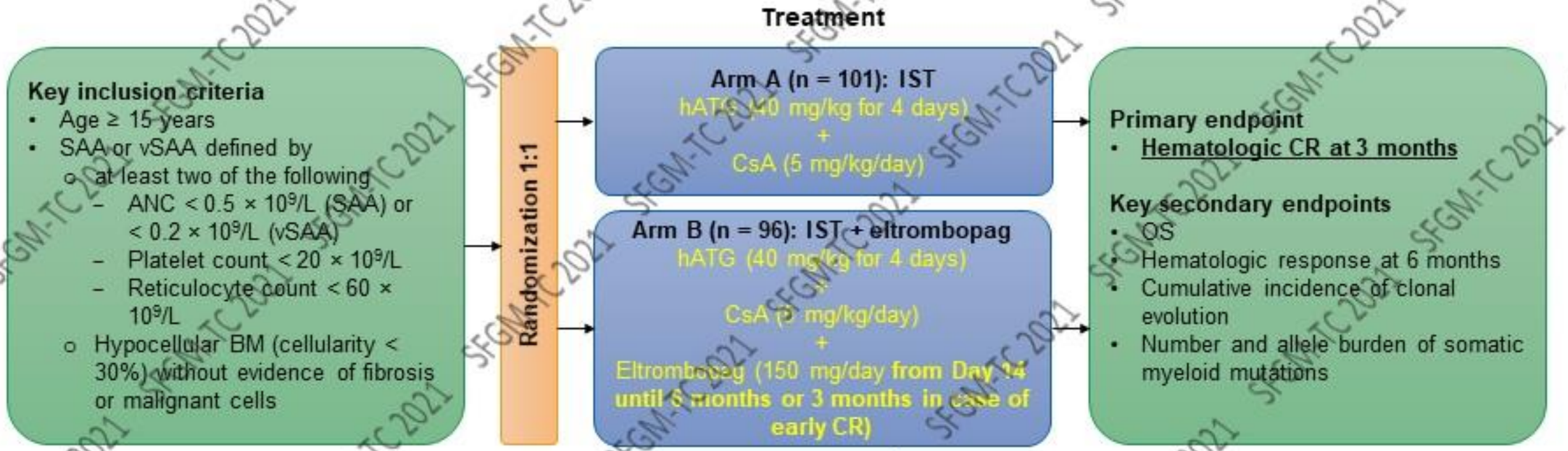




Schmitz et al.

# RACE trial

- The **RACE trial** is an investigator-driven, open-label, phase 3, randomized trial comparing the combination of horse ATG, CsA, and eltrombopag with IST alone in patients with SAA (26 sites, 6 countries)




**Central laboratory**: King's college, London; **Stratification** based on disease severity age and center

ANC, absolute neuthrophil count; vSAA, very severe aplastic anemia.

Peffault de Latour et al, *NEJM*, in press

EPAG, when added to standard IST (hATG and CsA), **significantly increases the rate of CR at 3 months** in untreated patients with SAA (primary endpoint)

**Time to first response** is significantly quicker (3 versus 8.8 months) and **overall response rate** is significantly higher (80% versus 66% at 6 months, NIH criteria)

**No safety concern** at time of analysis was identified (24 months median follow-up)

Notably **somatic myeloid mutations assessment** showed no difference between arms (occurrence and correlation with outcomes).

> EPAG at the top of horse ATG and CsA is the new standard of care for adult patients with SAA who are not eligible for transplantation.

Peffault de Latour et al, *NEJM*, in press

# CONCLUSIONS

PT-Cy ⟷ SAL greffes matchées

PT-Cy + MMUD (non rando)

CDT NMA: beaucoup de rechutes, surtout patho myéloïdes haplo ou cordon
NMA haplo > cordon

Préventif GVH: Rando: ATG MRD (+ GRFS , pas d'effet OS), Abatacept (+ survie sans GVHa)
Non rando: Sirolimus, Sitaglipine

GVH corticoR: Ruxo traitement de référence 2de ligne
Pas de bénéfice inhibiteur JAK1 en 1ere ligne
TMF: en 3ieme ligne?
ROCK inhibiteur: prometteur dans la GVHc cortico ref

→ jeudi 18/11/21
08:00 - 08:30
**Nouveautés dans le traitement de la GVH aiguë**
Edouard FORCADE (Bordeaux)

Rôle +++ MRD pré allo dans la LAM pour le prc post allo. Intérêt d'intensifier le CDT?

Rôle de la MRD dans les LALphi+: excellent devenir avec stratgie chémo free, intérêt de l'allo?

→ Mercredi 17/11/2113:30 - 14:00
**Quels traitements pré-allogreffes pour améliorer la MRD dans les LAM ?**
Thomas CLUZEAU (Nice)
14:00 - 14:30
**Quels traitements post-allogreffes : de l'immunomodulation aux traitements ciblés ?**
Didier BLAISE (Marseille

CART anti CD19 LAL ref/rec adulte? Moins bien que enfants, mais mieux que les alternatives médicamenteuses?

# CONCLUSIONS

PT-Cy ⟷ SAL greffes matchées

PT-Cy + MMUD (non rando)

CDT NMA: beaucoup de rechutes, surtout patho myéloïdes haplo ou cordon
NMA haplo > cordon

Préventif GVH: Rando: ATG MRD (+ GRFS , pas d'effet OS), Abatacept (+ survie sans GVHa)
Non rando: Sirolimus, Sitaglipine

GVH corticoR: Ruxo traitement de référence 2de ligne
Pas de bénéfice inhibiteur JAK1 en 1ere ligne
TMF: en 3ieme ligne?
ROCK inhibiteur: prometteur dans la GVHc cortico ref

Rôle +++ MRD pré allo dans la LAM pour le prc post allo. Intérêt d'intensifier le CDT?

Rôle de la MRD dans les LALphi+: excellent devenir avec stratgie chémo free, intérêt de l'allo?

CART anti CD19 LAL ref/rec adulte? Moins bien que enfants, mais mieux que les alternatives médicamenteuses?

Mercredi 17/11/21
18:15 - 18:45
**CAR T-Cells et LNH : les enseignements de l'année 2021**
Roch HOUOT (Rennes)
18:45 - 19:05
**CAR T-Cells et LNH : apports du laboratoire d'Immunologie**
Sophie CAILLAT-ZUCMAN (Paris)