SFGM TC
Société Francophone de GREFFE DE MOELLE et de Thérapie Cellulaire

Centre Hospitalier Régional Universitaire de Lille

Transplantation ASH 2015

Ibrahim Yakoub-Agha

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Université de Lille

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Pôle de Recherche et d'Enseignement Supérieur

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ASH 2015: Transplantation

- **Améliorer les résultats de l'allogreffe**
- **La greffe haploidentique**

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Impact of Early Post-Transplant Complications on Survival of Patients with Myelodysplastic Syndrome Undergoing Allo-SCT Following Reduced Intensity Conditioning: An SFGM-TC Study

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With the purpose of identifying factors that affect overall survival (OS), we conducted a retrospective multicenter study on a homogenous cohort.

Transplantation modalities were made as homogeneous as possible:

(i) Patients with MDS >18 years
(ii) first allo-SCT following RIC
(iii) with at least one year of follow-up
(iv) a sibling or an HLA-identical unrelated donor at allelic level (so called 10/10).

Patients: 275 consecutive.

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In multivariate analysis, 3-year OS was influenced by:

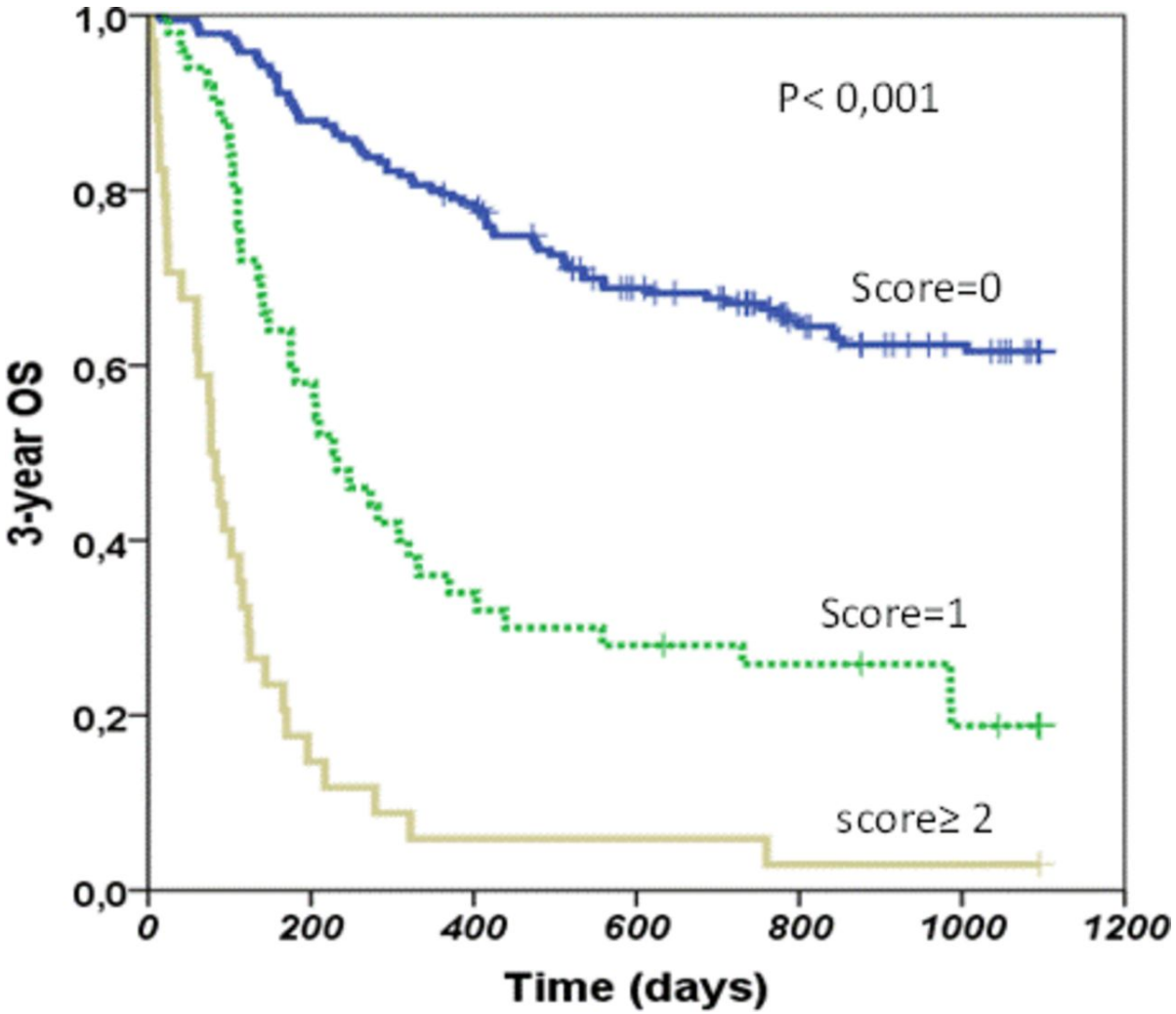
- platelet count ≥ 20G/L before d+100 [HR=**6.6**; CI95=4.1-10.6 ; p<0.001]
- grade III/IV acute GVHD [HR=**2.8** ; CI95=1.8-4.3 ; p<0.001],
- relapse before d+100 after transplant [HR=**3**; CI95=1.9-4.7 ; p<0.001),

A prognostic score:

Lack of platelet recovery	(2 points)
Grade III/IV acute GVHD	(1 point)
Relapse before d+100	(1point)

Three risk groups:

- **good** (score=0; n=191, 3-year OS=63%),
- **intermediate** (score=1; n=50; 3-year OS=20%)
- **poor** (score≥2; n=34; 3-year OS=3%).



Alexis Caulier et al. Blood 2015;126:1922

1. **Comment réduire l'incidence et la sévérité de la GVH**

2. **Comment améliorer le contrôle de la maladie après la greffe**

3. **Comment améliorer la prise de greffe**

blood

1. **Comment réduire l'incidence et la sévérité de la GVH**

2. **Comment améliorer le contrôle de la maladie après la greffe**

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Upper Gastrointestinal Acute Graft-Versus-Host Disease Adds Minimal Prognostic Value When Present in Isolation or in Addition to Grade I or Other Grade II-Defining GvHD Manifestations

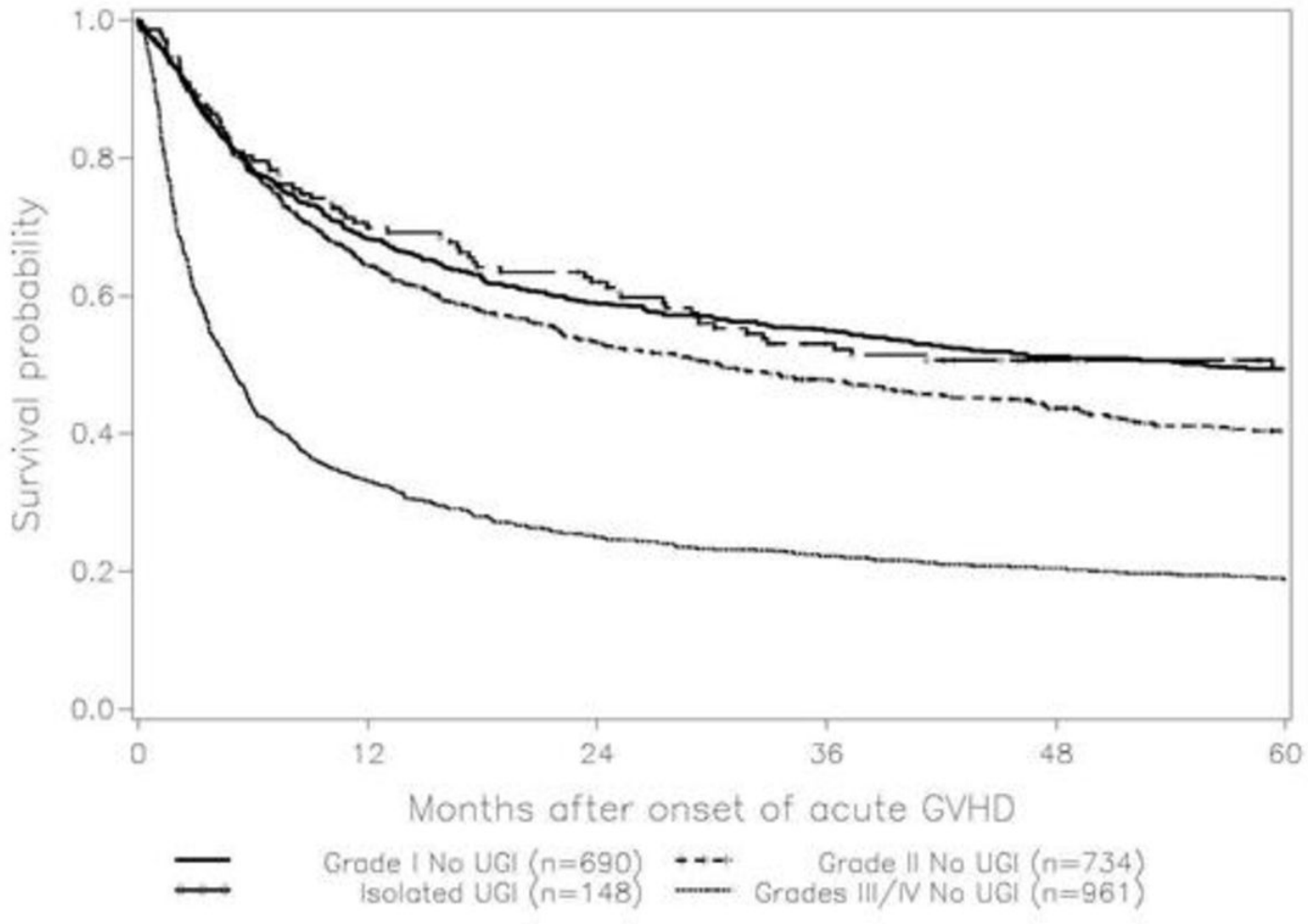
Sarah Nikiforow, MD PhD[1,2], Michael Hemmer, MS*[,3], Stephen R. Spellman, MBS*[,4], Amin M. Alousi, MD[5], Daniel R. Couriel, MD[6], Joseph A Pidala, MD, PhD[7], Mukta Arora, MD[8], Corey S Cutler, MD MPH[1], and Tao Wang, PhD*[,9]

Overall Survival - Isolated UGI aGvHD versus grades of aGvHD without UGI involvement.

MRD Recipients	HR	Range	p value
Isolated UGI (baseline)	1.00		
No aGvHD	1.03	0.71-1.49	0.85
Grade I	0.95	0.69-1.35	0.77
Grade II – no UGI	1.25	0.77-2.04	0.36
Grades III/IV – no UGI	2.51	1.71-3.68	**<0.0001**
URD Recipients	**HR**	**Range**	**p value**
Isolated UGI (baseline)	1.00		
No aGvHD	1.25	0.94-1.67	0.1223
Grade I	1.12	0.87-1.45	0.3821
Grade II – no UGI	1.59	1.08-2.33	0.0166
Grades III/IV – no UGI	2.88	2.16-3.83	**<0.0001**

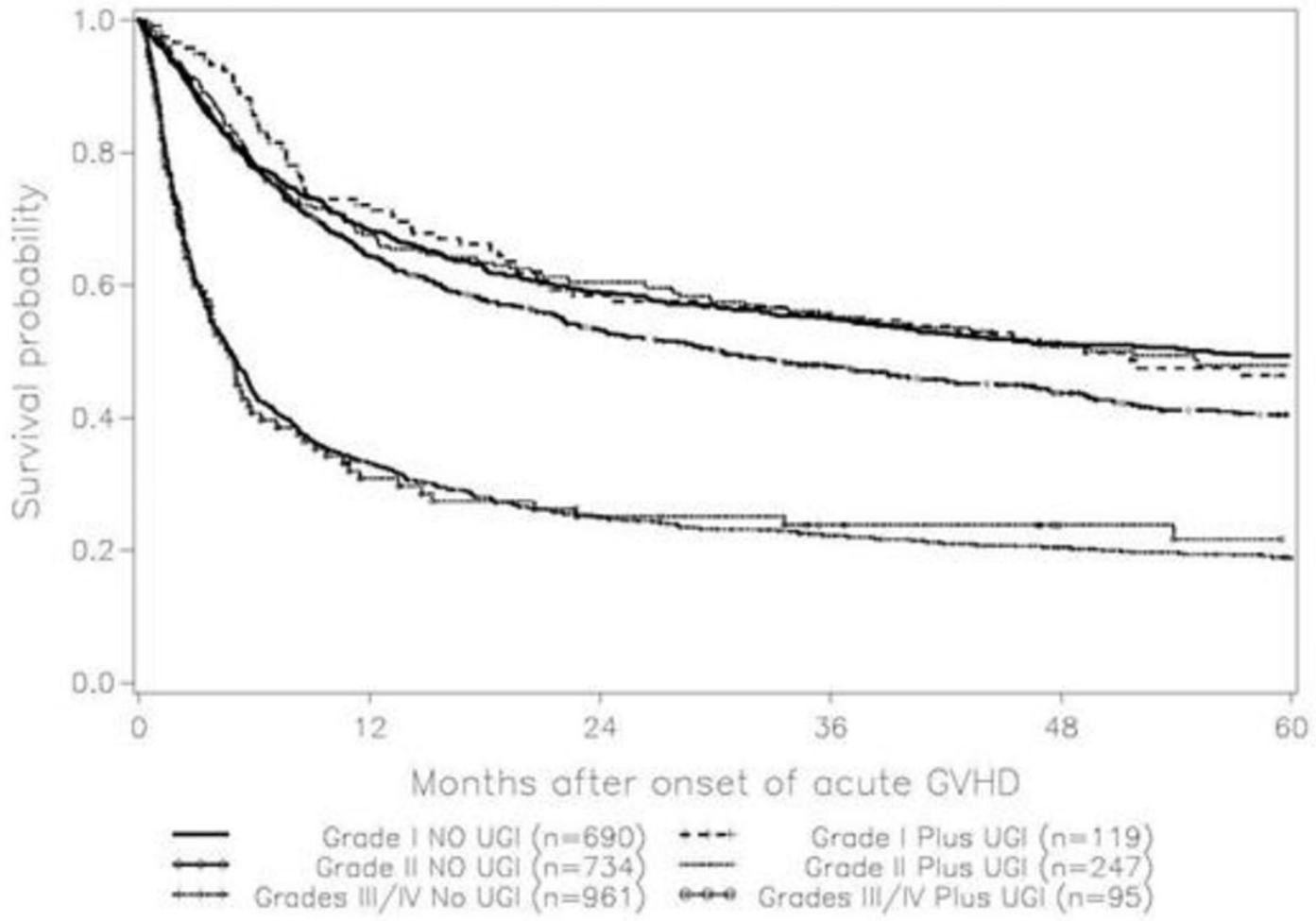
Sarah Nikiforow et al. Blood 2015;126:857

Survival for URD recipients with isolated UGI versus grades of aGvHD without UGI involvement.



Sarah Nikiforow et al. Blood 2015;126:857

Survival for URD recipients with aGvHD manifestations in addition to or without UGI symptoms.



Sarah Nikiforow et al. Blood 2015;126:857

A Bayesian, Phase II Randomized Trial of Extracorporeal Photopheresis (ECP) Plus Steroids Versus Steroids-Alone in Patients with Newly Diagnosed Acute Graft Vs. Host Disease (GVHD): The Addition of ECP Improves Gvhd Response and the Ability to Taper Steroids

Amin M. Alousi, MD[1], Roland Bassett, MS*,[2], Julianne Chen*,[1], Bethany J Overman, BSN*,[1], Chitra M. Hosing, MD[1], Uday R. Popat, MD[1], Elizabeth J. Shpall, MD[1], Yago Nieto, MD PhD[1], Muzaffar H. Qazilbash, MD[1], Issa F. Khouri[1], Partow Kebriaei, MD[1], Sairah Ahmed, MD[1], Nina Shah, MD[1], Katayoun Rezvani, MD, PhD[1], Kayo Kondo, PhD*,[1], Stefan O. Ciurea, MD[1], Sharon R Hymes, MD*,[3], Joyce L Neumann, APN, PhD*,[1], Jeffrey J. Molldrem, MD[1], Tamera R Plair, PA*,[1], and Richard E. Champlin, MD[1]

Treatment: 2mg/kg MP with or without ECP.
ECP schedule was: days 1-14 (8 sessions), days 15-28 (6 sessions) and days 29-56 (8 sessions).

Treatment: ECP + MP (51 pts) or MP-alone (30 pts).
Conditioning: MAC 69% and RIC 31%.

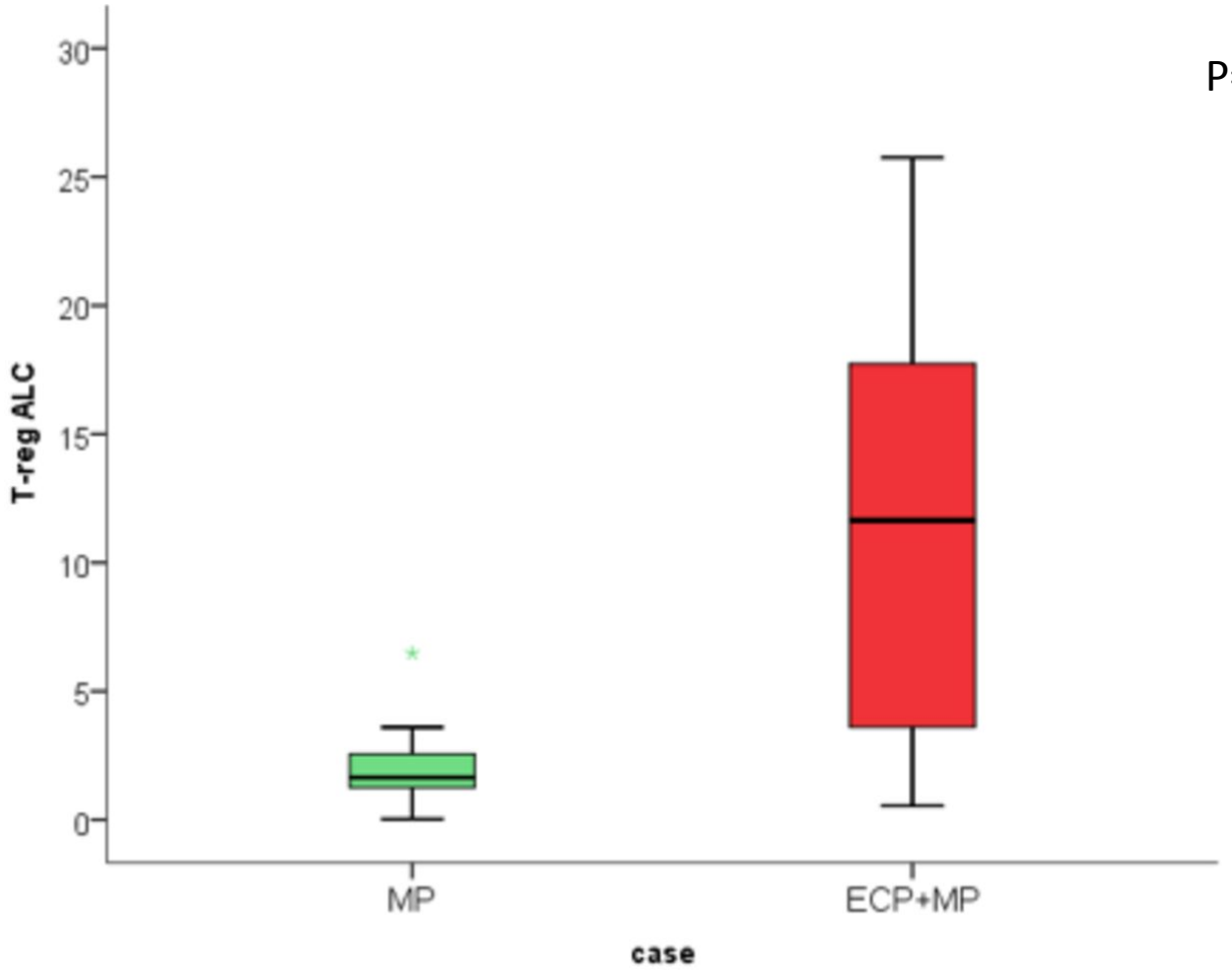
aGVHD: grade II (90%) , grade III/IV (10%).
Organ Involvement: skin (86%), upper GI (22%), lower GI (22%) and liver (10%).

The ECP-arm was more beneficial in pts with skin-only aGVHD (72% vs. 57% response rate) whereas visceral-organ involvement response rates were similar (47% vs. 43%).

By day 56, 43% of the evaluable patients randomized to the ECP were on physiologic doses of steroids (≤0.1mg/kg) versus 30% for MP-alone arm (p=0.034).

Conclusions: The results of this randomized, phase II trial indicate that the addition of ECP to steroids results in higher GVHD response and facilitates steroid-tapering in pts with newly diagnosed aGVHD.
This combination appears most efficacious for pts with skin-involvement.

Mean Absolute Regulatory T-cell Count in subset of patients randomized to ECP+MP (red) vs.



Amin M. Alousi et al. Blood 2015;126:854

Treatment of Corticosteroid-Refractory Graft-Versus-Host Disease with Ruxolitinib in 95 Patients

Robert Zeiser, MD[1], Andreas Burchert, MD[2], Claudia Lengerke, MD[3], Mareike Verbeek*,[4], Kristina Maas-Bauer, MD*,[5], Stephan Metzelder, MD*,[6], Silvia Spoerl, MD*,[7], Markus Ditschkowski, MD*,[8], Matyas Ecsedi, MD*,[9], Katja Sockel, MD*,[10], Francis Ayuk, MD*,[11], Salem Ajib, MD*,[12], Flore Sicre de Fontbrune, MD*,[13], Il-Kang Na, MD*,[14], Livius Penter, MD*,[15], Udo Holtick, MD PhD*,[16], Dominik Wolf, MD*,[17], Esther Schuler, MD*,[18], Everett Meyer, MD PhD[19], Petya Apostolova, MD*,[20], Hartmut Bertz, MD*,[21], Reinhard Marks[22], Michael Luebbert, MD*,[23], Ralph M. Waesch, MD PhD[24], Christof Scheid, MD PhD[25], Friedrich Stölzel, MD*,[10], Rainer Ordemann, MD*,[26], Gesine Bug, MD*,[27], Guido Kobbe, MD*,[28], Robert Negrin, MD[29], Mats L Brune[30], Alexandros Spyridonidis[31], Annette Schmitt-Graeff, MD*,[32], Walter van der Velden, MD*,[33], Gerwin Huls, MD PhD*,[34], Stephan Mielke, MD[35], Goetz Ulrich Grigoleit, MD*,[36], Jurgen Kuball, MDPhD[37], Ryan P Flynn, PhD*,[38], Gabriele Ihorst, PhD*,[39], Jing Du[40], Bruce R. Blazar, MD[41], Renate Arnold, MD[15], Nicolaus Kröger, MD*,[42], Joerg Halter, MD*,[43], Gerard Socie[44], Dietrich Beelen, MD[45], Christian Peschel, MD[46], Andreas Neubauer, MD[6], Juergen Finke, MD[47], Justus Duyster, MD PhD*,[48], and Nikolas von Bubnoff, MD*,[23]

Background: Pre-clinical evidence indicates the potent anti-inflammatory properties of the JAK1/2 inhibitor *ruxolitinib* by modification of T cells and dendritic cells.

Methods: In this retrospective analysis, 95 patients
Treatment: ruxolitinib as salvage-therapy for SR-GVHD.

- grade III-IV acute GVHD (n=54)
- cGvHD (n=41, all moderate or severe).

	Acute GVHD	Chronic GVHD
ORR	82%	84%
Time to response	1.5 weeks (1-11)	3 weeks (1-25)
GVHD-relapse	7%	6%
6-month OS	79%	97%
Cytopenia	56%	17%
CMV reactivation	33%	15%
Relapse of UD	9%	2%

Conclusion: Ruxolitinib constitutes a promising new treatment option for SR-aGVHD and SR-cGVHD. Its activity in SR-aGVHD and SR-cGVHD should be validated in a prospective trials in both, SR-aGvHD and cGvHD.

ATG and Statins Reduce Incidence of Severe Chronic Gvhd By Distinct Mechanisms Involving CXCL9 and Kynurenine Catabolism

Thomas Luft, MD PhD[1], Katharina Schmidt, MD*,[2], Karl-Heinz Kellner, PhD*,[3], Aleksandar Radujkovic, MD*,[1], Nicola Lehners, MD*,[4], Mark-Alexander Schwarzbich, MD*,[5], Ute Hegenbart, MD*,[1], Anthony D. Ho, MD[6], and Peter Dreger, MD[1]

Anthranilic acid (AA) reduces the severity of acute GVHD in mice.

AA is the product of a complex metabolic pathway involving

- indoleamine 2,3-dioxygenase (IDO),
- kynurenine (Kyn),
- Vitamin B6.

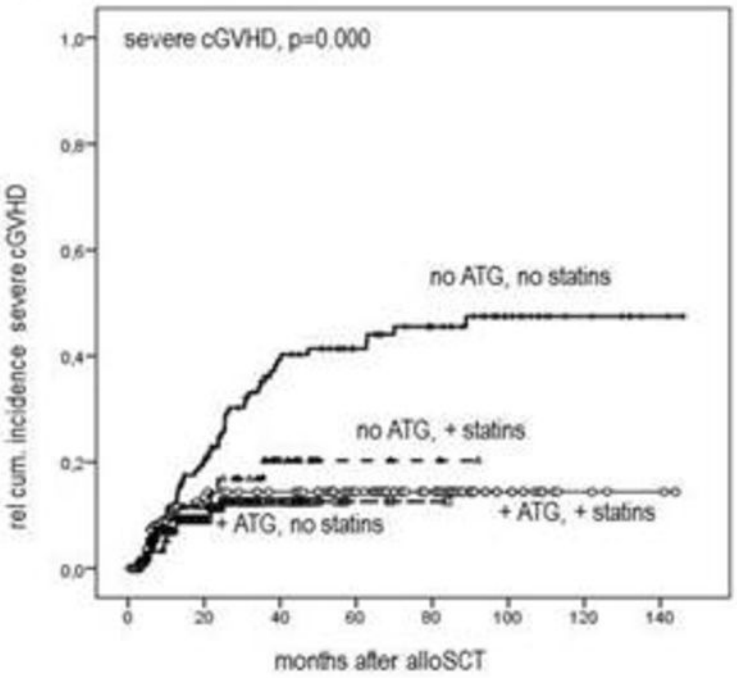
- anti-thymocyte globulin (ATG) and statins independently reduce the incidence of severe cGVHD.

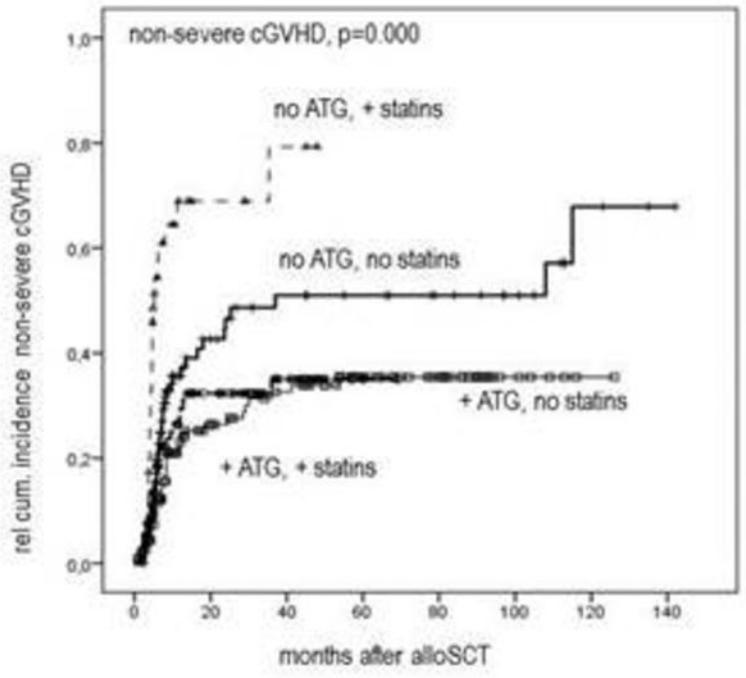
Observational study: 554 patients who survived the first 6 months after allo-SCT.
Median age was 53 years.
Donors were matched related (194), matched unrelated (227), mismatched unrelated (113), or haploidentical (15).

Conditioning: MAC (n=101), RIC (n=453) patients.

ATG (n=325), pravastatin at a dose of 20 mg/d starting from day-1 (n=244), both (n=176) and none (n=159).

Day +100 serum samples for measuring CXCL9, IDO, Trp and Kyn by ELISA were available for **350** patients and at onset of cGVHD for **185** patients.





Thomas Luft et al. Blood 2015;126:856

Conclusions: Our data suggest that ATG and statins minimize severe cGVHD by distinct mechanisms.

Mesenchymal Stem Cell As a Salvage Treatment for Patients with Refractory Bronchiolitis Obliterans Syndrome after Allogenetic Hematopoietic Stem Cell Transplantation

Ke Zhao, MD*,[1], Zhiping Fan, MD*,[2], Fen Huang*,[3], Peng Xiang, PhD*,[4], and Qifa Liu, MD[1]

Prospective study.

Patients: 53 pts with refractory BOS. MSC group (n=29) and in non-MSC group (n=24).

All patients had previously failed to at least 2 lines of immunosuppressive therapy.

MSCs were given at a median dose of 1×10^6 cells/kg once weekly X 4 weeks.

The responsiveness of MSC was evaluated after one cycle, non-responsive patients discontinued MSC treatments, others continued to accept another cycle of MSC treatments.

Median of cycles = 6 (range:3-11)

Results

	MSC group	No-MSC	P
ORR	76%	17%	0.000
CR	14%	4%	0.233
PR	62%	13%	0.000
Deaths	7 pts	18 pts	
5-year 0S	67%	21%	0.033
Other toxicity	0	0	

Conclusion MSC derived from BM of third-party donors is a promising treatment for patients with refractory BOS.

1. Comment réduire l’incidence et la sévérité de la GVH

2. **Comment améliorer le contrôle de la maladie après la greffe**

3. Comment améliorer la prise de greffe

Fludarabine Busulfan Compared to Fludarabine Melphalan Is Associated with Increased Relapse Risk in Reduced Intensity Conditioning Transplant Despite Pharmacokinetic Dosing

Moussab Damlaj, MD[1], Hassan B Alkhateeb, MD*,[1], Daniel K. Partain, MD*,[2], Jehad Almasri, MD*,[3], Mehrdad Hefazi, MD*,[2], Shahrukh K. Hashmi, MD[1], Dennis A. Gastineau, MD[4], Aref Al-Kali, MD[3], Robert C Wolf, PharmD[5], Naseema Gangat, MBBS[1], Mark R Litzow, MD[1], William J Hogan, MBChB[1], and Mrinal M Patnaik, MBBS[1]

Aim: Compare transplant related outcomes of FB vs. FM using intravenous (IV) busulfan targeted to the area under the curve (AUC).

Table 1. Baseline characteristics of patients stratified by conditioning

	Flu-Bu (n = 47)	Flu-Mel (n = 87)	p value
Patient age in years, median (range)	60 (18-67)	61 (33-72)	0.015
Recipient gender, male n (%)	29 (62)	55 (63)	1.0
Time from dx to HSCT in days, median (range)	223 (31-1897)	170 (16-5905)	0.48
Diagnosis, n (%)			1.0
AML	34 (72)	63 (72)	
MDS	13 (28)	24 (28)	
Secondary / therapy related disease	13 (38)	29 (33)	0.56
Status at HSCT, n (%)			0.53
CR1	32 (68)	67 (77)	
CR2	9 (19)	12 (14)	
Advanced	6 (13)	8 (9)	
Cytogenetics, n (%)			0.29
Favorable	2 (4)	3 (3)	
Intermediate	27 (57)	54 (62)	
High risk	18 (38)	30 (34)	
Female donor / Male recipient, n (%)	11 (24)	22 (26)	0.83
Donor Source, n (%)			0.59
Related	24 (51)	49 (56)	
Unrelated	23 (49)	38 (44)	
Stem Cell Source, n (%)			0.42
PBSCT	46 (98)	81 (93)	
BM	1 (2)	6 (7)	
HLA Matching, n (%)			0.66
Matched	46 (98)	82 (94)	
Mismatched	1 (2)	5 (6)	
ABO Matching, n (%)			0.19
Match	35 (74)	52 (60)	
Major / Bidirectional	8 (17)	19 (22)	
Minor	4 (8.5)	16 (18)	
CMV status, n (%)			0.064
D+/R+, D+/R- or D-/R+	34 (72)	75 (86)	
CMV R-/D-	13 (28)	12 (14)	
Immunosuppression, n (%)			0.47
CsA and MTX			
Tac and MTX	23 (49)	49 (57)	
	24 (51)	37 (43)	

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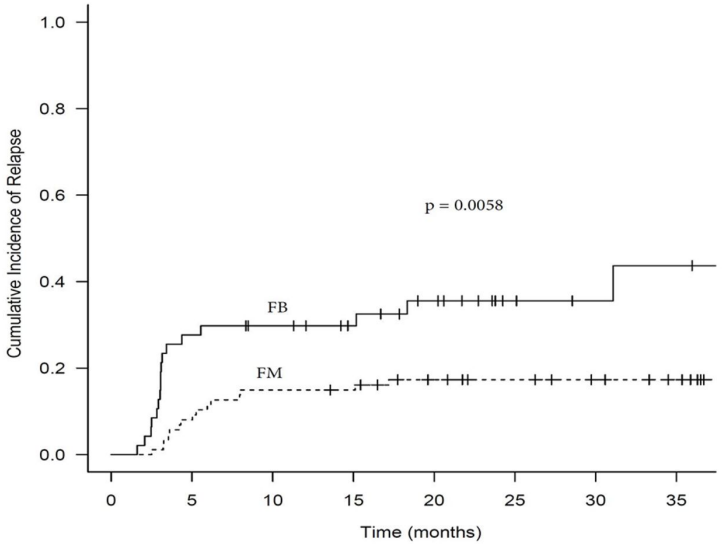
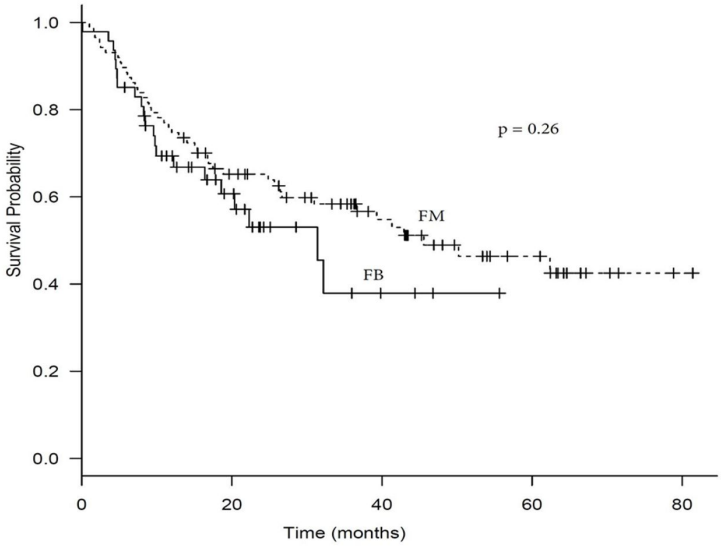
Results

	FB	FM	*p*
Plaquettes	19 j	16 j	0,077
PNN	18 j	15 j	0.0023
Relapse	37%	17%	0,0058
EFS	51%	65%	0,031
aGVHD II-IV	57%	47%	ns
aGVHD III-IV	11%	17%	ns
cGVHD	53%	63%	ns





Conclusion: Despite AUC dose adjustment, FB compared to FM was associated with increased RI with a similar OS and NRM.

AUC dose adjustment did not impact transplant outcomes and its routine use in RIC should be further evaluated.

Given the wide use of FB as a conditioning regimen, these important observations should be prospectively studied in a randomized fashion.

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A Phase I Trial of Total Marrow and Lymphoid Irradiation (TMLI)-Based Transplant Conditioning in Patients (Pts) with Relapsed/Refractory Acute Leukemia

Anthony Selwyn Stein, MD[1], Jeffrey Y. C. Wong, MD*,[2], Joycelynne Palmer, PhD*,[3], Margaret O'Donnell, MD[4], David S. Snyder, MD[5], Ni-Chun Tsai, Biostatition*,[6], Pablo Miguel Parker, MD[7], Ricardo Spielberger, MD[8], Len Farol, MD*,[9], Guido Marcucci, MD[10], Eric Radany, MD*,[11], Tim Schultheiss, MD*,[12], An Liu, MD*,[12], Ibrahim Aldoss, MD[13], and Stephen J. Forman, MD[1]

Conditioning: 20 Gys TMLI/CY/VP16
Median follow-up: 23.5 months
1-year NRM: 8.3%
1-year OS: 54.4% respectively
Relapsed: 33 patients (bone marrow, 26; extramedullary disease, 6; concurrent bone marrow/extramedullary, 1).
Acute GVHD : 55% II-IV including 14% III-IV

Conclusion: A dose of 2000 cGy targeted to lymph nodes and marrow in combination with CY and VP16 can be safely administered in the context of related and unrelated HCT, using tacrolimus and sirolimus for GVHD prophylaxis. We did not see increased incidence of aGVHD, and the day +100 NRM rate was <5%. A phase II trial is currently being conducted.

Variable	Median (range) or N
Age at transplant (yrs)	34 (16-57)
Disease diagnosis	33
AML	13
ALL Ph-	2
ALL Ph+	2
biphenotypic	1
undifferentiated	
Disease status at HSCT	14
1 RL	3
2 RL	34
IF	
Cytogenetic risk (SWOG criteria)	1
favorable	22
intermediate	19
unfavorable	9
unknown significance	
KPS at HSCT	80 (60-100)
Donor source	25
sibling	5
HLA matched unrelated	21
mismatched (1 allele) unrelated	
WBC at HSCT	1.4 (0.1-14.9)
% Blasts in blood at transplant*	4 (0-93)
% Blasts in marrow at transplant*	52 (8-98)
Extramedullary disease at time of HSCT	11

*Excludes patients with solely extramedullary disease, n=4

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3. **Comment améliorer la prise de greffe**

Eltrombopag for Post-Transplant Thrombocytopenia: Results of Phase II Randomized Double Blind Placebo Controlled Trial

Uday R. Popat, MD[1], Genevieve Ray*,[2], Roland L Bassett Jr.*,[2], Man-Yin C Poon*,[1], Benigno C. Valdez, PhD[1], Sergej Konoplev, MD PhD[3], Sairah Ahmed, MD[1], Amin M. Alousi, MD[1], Borje Andersson, MD PhD[1], Qaiser Bashir, MD*,[1], Stefan O. Ciurea, MD[1], Chitra M. Hosing, MD[1], Roy Jones, MD PhD*,[1], Partow Kebriaei, MD[1], Issa F. Khouri, MD[1], Stella Kim*,[4], Yago Nieto, MD PhD[1], Amanda L. Olson, MD*,[1], Betul Oran, MD[1], Simrit Parmar, MD[1], Muzaffar H. Qazilbash, MD[1], Katy Rezvani, MD PhD*,[1], Nina Shah, MD[1], Elizabeth J. Shpall, MD[1], and Richard E. Champlin, MD[1]

Inclusion: > 35 post-transplant

1) platelet count ≤ 20 x 10^9/l sustained for 7 days or if they were platelet transfusion dependent, and
2) neutrophil count ≥ 1.5 x 10^9/l with or without G-CSF in the previous 7 days.

Exclusion:

1) abnormal liver function tests (ALT ≥ 2.5 ULN, or Bilirubin >2mg/dl)
2) prior venous thrombosis.

Patients were randomized to receive placebo (n=18) or eltrombopag (n=42) (started at 50mg and escalated every 2 weeks to 75mg, 125 mg and 150mg if platelet count was < 50 x 10^9/l.)

Results: 7 (autograft) and 53 (allografts).
Stem cell source was PBSC in 36 patients, BM in 23 patients and cord blood in 1 patient.
15 (36%) of patients in eltrombopag arm responded compared to 5 (28%) of patients in placebo arm.
Achieving a platelet count ≥ 50 x 10^9/l.
eltrombopag arm 9 (21.4%) and placebo 0 (0%) (p=0.0466; Fisher's exact test).
OS, PFS, relapse rate, and non-relapse mortality were similar in two arms.

Conclusion: Eltrombopag improves platelet count in patients with post-transplant thrombocytopenia.

ASH 2015: Transplantation

- Améliorer les résultats de l'allogreffe

- **La greffe haploidentique**

blood

1. **Indication**
2. **Haplo versus donneur alternatif**
3. **Quel donneur?**
4. **Quelle source de CSH?**

blood

1. **Indication**
2. Haplo versus donneur alternatif
3. Quel donneur?
4. Quelle source de CSH?

Stem-Cell Transplantation in Adults with Philadelphia-Negative High-Risk Acute Lymphoblastic Leukemia in First Complete Remission: A Prospective Multicenter Trial Comparing Haploidentical Donors with Identical Sibling Donors

Yu Wang*,[1], Wu Depei[2], Qifa Liu, MD[3], Lan-Ping Xu*,[1], Xiao-Hui Zhang*,[1], and Xiao-Jun Huang, MDPhD[4]

LAL PH1nég en RC1

Randomisation génétique: 103 haplo et 83 fratrie HLA-identique

Conditionnement: basé sur l'ATG (10 mg/kg)

Greffon: G-CSF puis MO et CSP

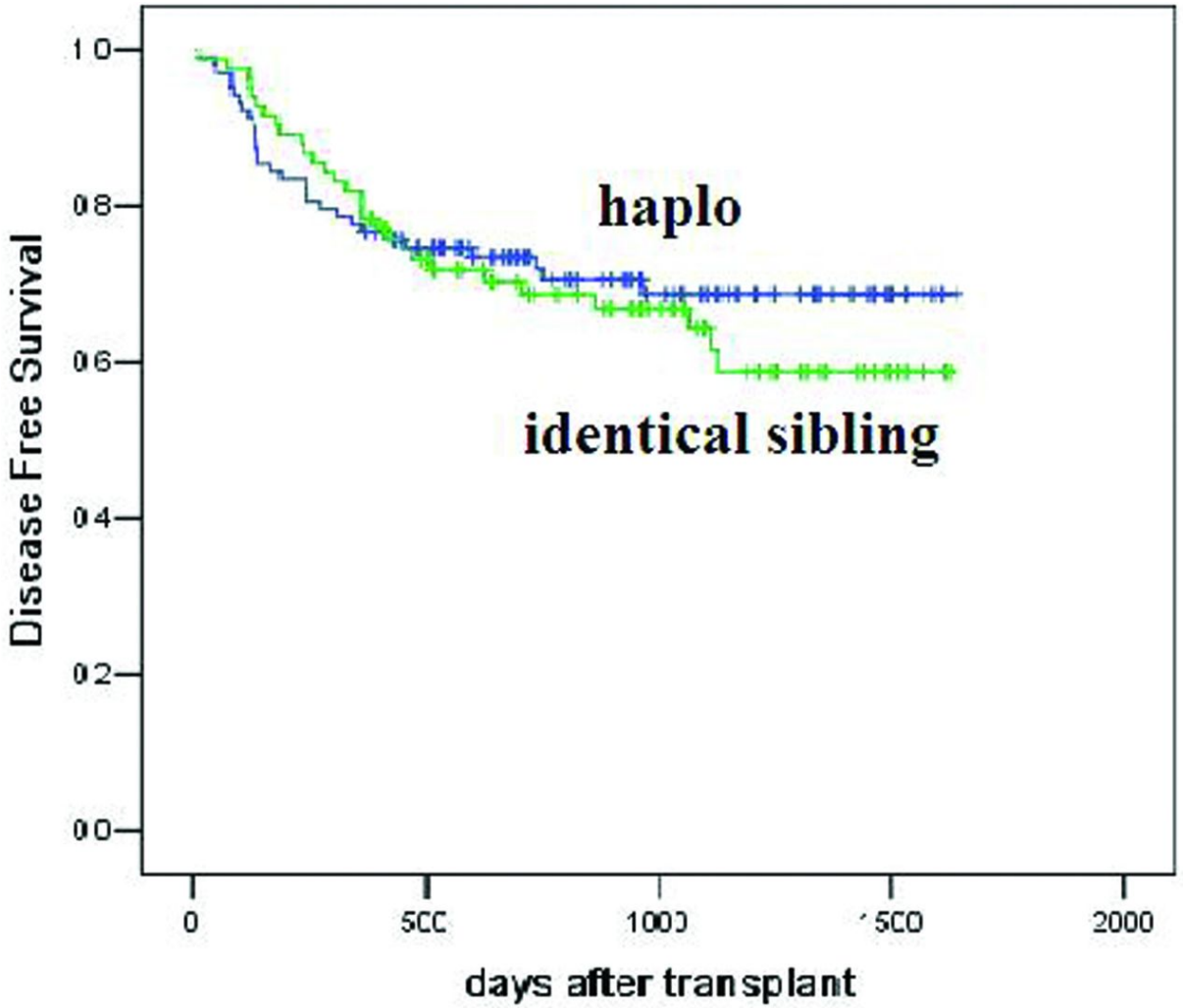
Prophylaxie de la GVH: Cs-A, MMF et MTX

Résultats à 3 ans (Haplo et fratrie)

- DFS: 68% et 64% (P =.56)
- OS: 75% et 69% (P = .51)
- Rechute: 18% et 24% (P = .30)
- NRM: 13% et 11% (P = .84)

- Prise de greffe: 99% pour les deux groupes

Outcome	Hazard ratio (95%Confidence interval)	p value
Disease free survival		
Haploidentical vs Identical sibling	0.88 (0.50-1.53)	.65
Patient age <30 vs >30 years	0.74 (0.42-1.28)	.28
Patient sex male vs female	1.13 (0.55-2.30)	.74
Time to transplant <6 vs >6 months	1.48 (0.86-2.56)	.16
Female-to-male vs other sex pair	0.95(0.52-1.75)	.86
Limited chronic GVHD vs no or extended	0.59 (0.29-1.17)	.13
Overall survival		
Haploidentical vs Identical sibling	0.91 (0.50-1.70)	.77
Patient age <30 vs >30 years	0.60 (0.33-1.11)	.11
Patient sex male vs female	1.13 (0.55-2.30)	.74
Time to transplant <6 vs >6 months	1.64 (0.89-3.01)	.11
Female-to-male vs other sex pair	1.22 (0.64-2.31)	.54
Limited chronic GVHD vs no or extended	0.59 (0.27-1.28)	.18
Relapse		
Haploidentical vs Identical sibling	0.67(0.33-1.36)	.27
Patient age <30 vs >30 years	1.06 (0.50-2.28)	.87
Patient sex male vs female	1.52 (0.64-3.62)	.35
Time to transplant <6 vs >6 months	1.42 (0.69-2.90)	.33
Female-to-male vs other sex pair	0.61(0.26-1.45)	.27
Limited chronic GVHD vs no or extended	0.65 (0.26-1.62)	.36
Non-Relapse-Mortality		
Haploidentical vs Identical sibling	1.38(0.58-3.35)	.46
Patient age <30 vs >30 years	0.47 (0.19-1.17)	.11
Patient sex male vs female	0.66 (0.19-2.33)	.52
Time to transplant <6 vs >6 months	1.66 (0.70-3.92)	.25
Female-to-male vs other sex pair	1.53(0.64-3.69)	.34
Limited chronic GVHD vs no or extended	0.63 (0.21-1.86)	.40



Yu Wang et al. Blood 2015;126:62

Haploidentical Hematopoietic Stem Cell Transplantation for Acquired Severe Aplastic Anemia

Miao Miao*,[1], Xiang Zhang*,[1], Ting Xu*,[1], Song Jin*,[1], Hong Wang*,[1], Xiaofei Yang*,[1], Zhijuan Pan*,[1], Jun He*,[1], Aining Sun, PhD*,[1], and Wu Depei, MD[1]

38 aplasies médullaires (36 cordons plus haplo)

Médiane de suivi: 11 mois (0-36)

Prise de greffe: PNN 12 jours (9-28)

GVHII-IV: 9%

Survie globale: 83%

1. Indication

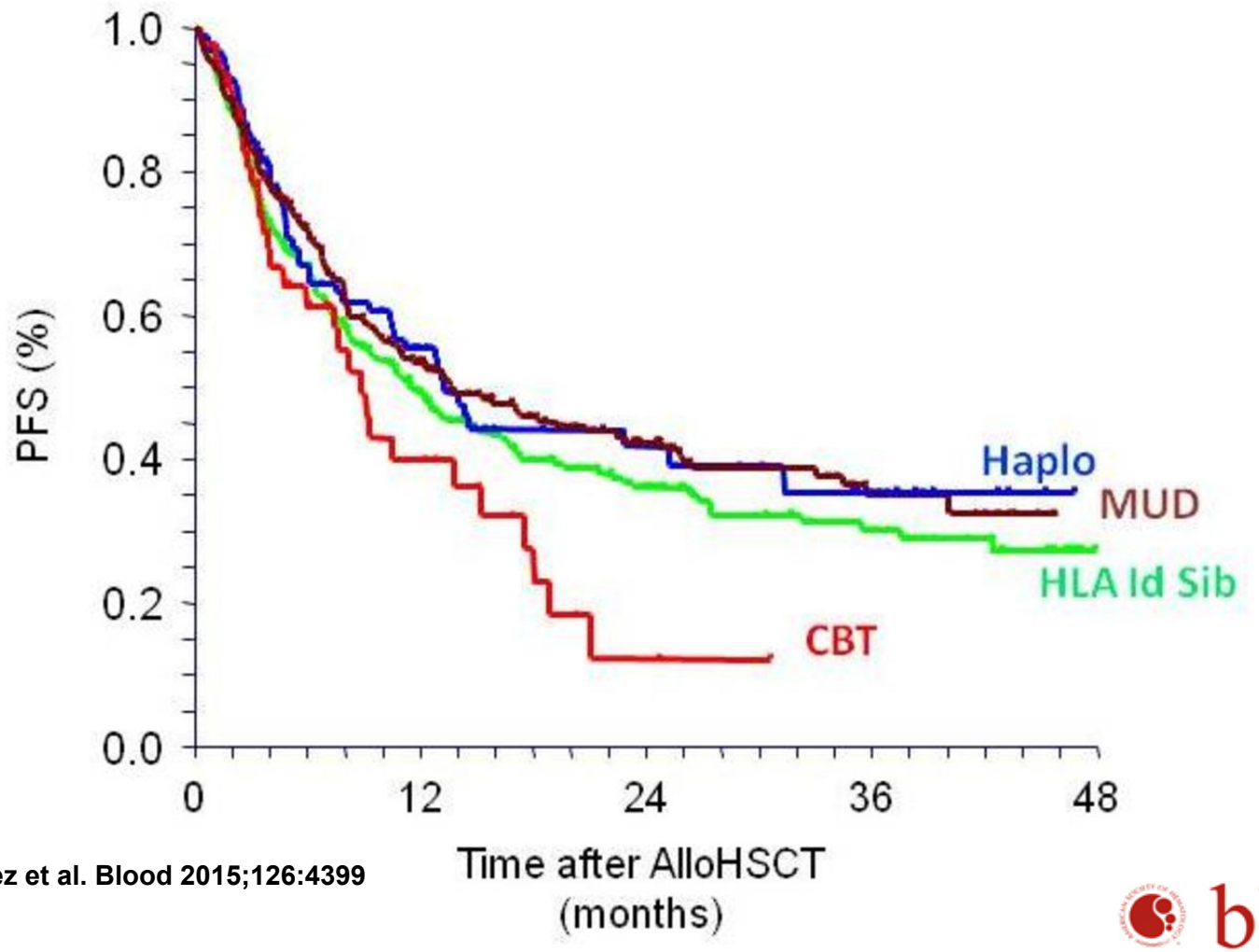
2. **Haplo versus donneur alternatif**

3. Quel donneur?

4. Quelle source de CSH?

Alternative Donors (Umbilical Cord Blood and Haploidentical Donors) for Allogeneic Stem Cell Transplantation in Relapsed / Refractory Hodgkin Lymphoma: A Retrospective Analysis of the EBMT Lymphoma Working Party and the Spanish Group of Stem Cell Transplantation (GETH)

Carmen Martinez, MD PhD*,[1], Jorge Gayoso, MD*,[2], Carmen Canals, MD PhD*,[3], Herve Finel*,[4], Andrea Bacigalupo, MD[5], Karl Peggs, MBBChir, MRCP, FRCPath*,[6], Noel Milpied[7], Fabio Ciceri, MD*,[8], Gerard Socie[9], Paolo Corradini, MD[10], Stephen Robinson*,[11], Andrea Velardi, MD[12], Nathalie Fegueux, MD*,[13], Gonzalo Gutierrez*,[14], Stephen Mackinnon, MD[15], Michael Potter[16], Boris Afanasiev*,[17], Jorge Sierra, MD PhD[18], Ram Malladi*,[19], Miguel A. Sanz, MD PhD[20], Nigel H. Russell, MD[21], William Arcese, MD[22], Vanderson Rocha, MD PhD[23], Peter Dreger, MD[24,25], and Anna Sureda, MD PhD*,[26]



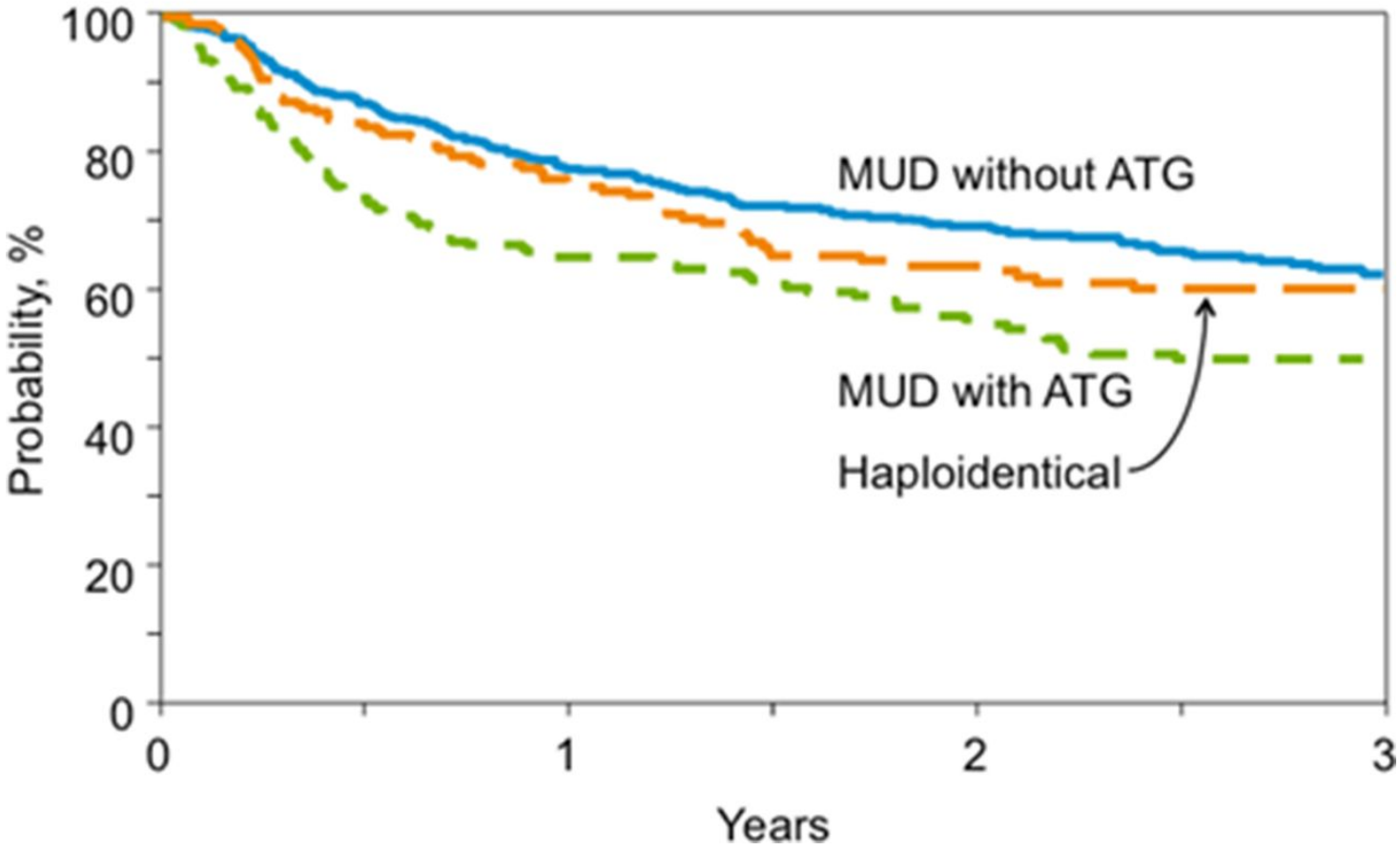
Carmen Martinez et al. Blood 2015;126:4399

Survival after T-Cell Replete Haploidentical Related Donor Transplant Using Post-Transplant Cyclophosphamide Compared with Matched Unrelated Donor (MUD) Transplant for Lymphoid Malignancies

Alberto Mussetti, MD*,[1], Abraham Sebastian Kanate, MD[2], Mohamed A Kharfan-Dabaja, MD[3], Kwang Woo Ahn, PhD*,[4], Alyssa DiGilio, MS*,[4], Stefan O Ciurea, MD[5], Philippe Armand, MD PhD[6], Rachel B. Salit, MD[7], Timothy S. Fenske, MD MS*,[8], Sonali M. Smith, MD[9], Anna Sureda, MD PhD*,[10], Javier Bolanos-Meade, MD*,[11], and Mehdi Hamadani, MD[12]

	Haploidentical N=185 (%)	MUD w/o ATG N=491 (%)	MUD w/ ATG N=241 (%)	p-value
Age @ HCT, median (range)	55 (18-75)	55 (19-74)	55 (20-73)	0.13
Male sex	118 (64)	301 (61)	163 (68)	0.25
White race	149 (81)	469 (96)	227 (94)	<0.001
KPS ≥ 90	145 (78)	311 (63)	153 (63)	<0.001
HCT-CI≥3	55 (30)	175 (36)	88 (37)	<0.001
Histology NHL Hodgkin	139 (75) 46 (25)	386 (79) 105 (21)	193 (80) 48 (20)	<0.001
Months from diagnosis to HCT, median (range)	31 (<1-255)	34 (<1-342)	32 (4-460)	0.19
High LDH @ HCT	16 (31)	31 (33)	11 (27)	<0.001
BM +ve @ HCT	6 (12)	5 (5)	2 (5)	0.35
Extranodal disease @ HCT	18 (35)	20 (21)	6 (15)	0.11
Prior lines of therapy, median (range)	3 (1-7)	3 (1-12)	3 (1-8)	0.41
Remission @ HCT CR PR Refractory Untreated / missing	72 (39) 99 (54) 10 (5) 4 (2)	215 (44) 215 (44) 55 (11) 6 (1)	100 (41) 96 (40) 40 (17) 5 (2)	0.02
Disease Risk Index Low Intermediate High	45 (24) 126 (68) 13 (7)	199 (41) 263 (49) 48 (10)	75 (31) 129 (54) 37 (15)	<0.001
Median follow-up, months (range)	36 (5-73)	35 (4-74)	35 (<1-75)	

Overall Survival

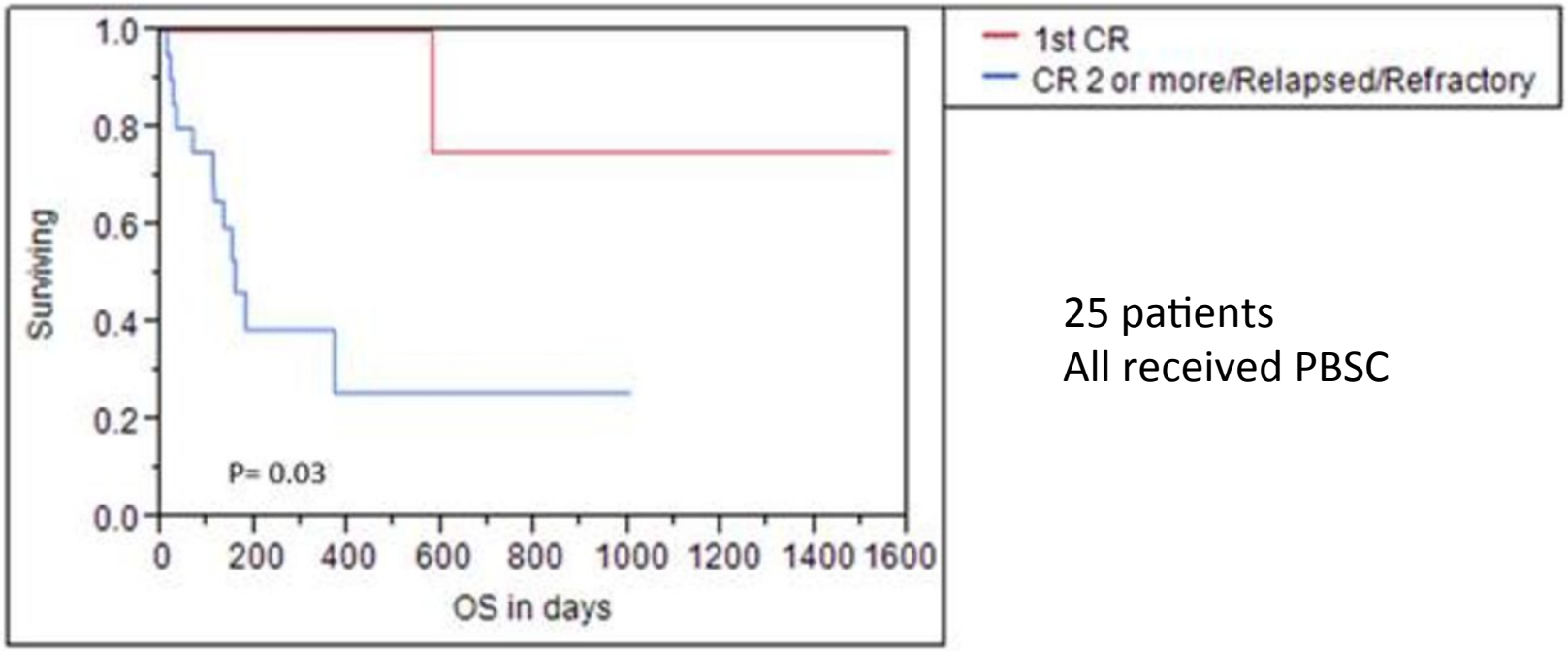


Alberto Mussetti et al. Blood 2015;126:194

Outpatient Haploidentical Peripheral Blood Stem-Cell Transplantation with Post-Transplant Cyclophosphamide in Children and Adolescents

Oscar Gonzalez-Llano, MD PhD*,[1], Elias Eugenio Gonzalez-Lopez, MD*,[2], Ana Carolina Ramirez-Cazares, MD*,[2], Edson Rene Marcos-Ramirez, MD*,[2], Guillermo J. Ruiz-Arguelles, MD FRCP (Glasg), MACP[3], and David Gomez-Almaguer, MD[4]

Figure 2 Patients transplanted of 1st CR vs patients transplanted on CR ≥2 or relapsed/refractory



25 patients
All received PBSC

Oscar Gonzalez-Llano et al. Blood 2015;126:4389

blood

Results of a Two-Arm Phase II Clinical Trial Using Post-Transplantation Cyclophosphamide for Prevention of Graft-Versus-Host Disease in Haploidentical and Mismatched Unrelated Donors Hematopoietic Stem-Cell Transplantation

Sameh Gaballa, MD[1], Isabell Ge*,[2], Riad O. El Fakih, MD*,[1], Jonathan E. Brammer, MD[1], Sa A. Wang, MD*,[3], Dean A. Lee, MD PhD[4], Demetrios Petropoulos, MD[4], Kai Cao, MS, MD*,[5], Gabriela Rondon, MD[1], Julianne Chen*,[1], Aimee E Hammerstrom, PharmD, BCOP*,[1], Gheath Al-Atrash, MD PhD*,[1], Martin Korbling, MD*,[1], Betul Oran, MD[1], Partow Kebriaei, MD[1], Sairah Ahmed, MD[1], Nina Shah, MD[1], Katayoun Rezvani, MDPhD[1], David Marin, MD*,[1], Qaiser Bashir, MD[1], Amin M. Alousi, MD[1], Yago Nieto, MD PhD[1], Muzaffar H. Qazilbash, MD[1], Chitra M. Hosing, MD[1], Uday R. Popat, MD[1], Elizabeth J. Shpall, MD[1], Issa F. Khouri[1], Richard E. Champlin, MD[1], and Stefan O. Ciurea, MD[1]

FM140: (> 55 or comorbidities)
- MEL 140 mg/m^2 (day -7),
- Thiotepa 5 mg/kg (day -6), (or TBI 2Gys)
- fludarabine 40 mg/m^2 (day -5 to day -2)

FM100: (> 55 or comorbidities)
- MEL 100 mg/m^2 (day -7),
- Thiotepa 5 mg/kg (day -6), (or TBI 2Gys)
- fludarabine 40 mg/m^2 (day -5 to day -2)

Rituximab (375 mg/m^2) on days -13, -6, +1 and +8: pts with CD20-positive NHL
GVHD prophylaxis : consisted of PTCy 50 mg/kg on day +3 and +4, and tacrolimus and mycophenolate for 6 and 3 months (mo), respectively.
The stem cell source: bone marrow.

	HAPLO (n=60)	9/10 MUD (n=46)
Median Age, years (Range)	45 (20-63)	51 (20-64)
Sex (M/F)	29/31	23/23
KPS		
≥90	53 (88%)	40 (87%)
<90	7 (12%)	6 (13%)
HCT-CI		
0-3	50 (83%)	38 (83%)
>3	10 (17%)	8 (17%)
Disease Risk Index*		
Very high	5 (8%)	3 (7%)
High	18 (30%)	15 (33%)
Intermediate	29 (48%)	12 (26%)
Low	8 (13%)	12 (26%)
NA	0	4 (9%)**
Conditioning Regimen		
FM100	20 (33)	18 (39%)
FM140	40 (67%)	28 (61%)

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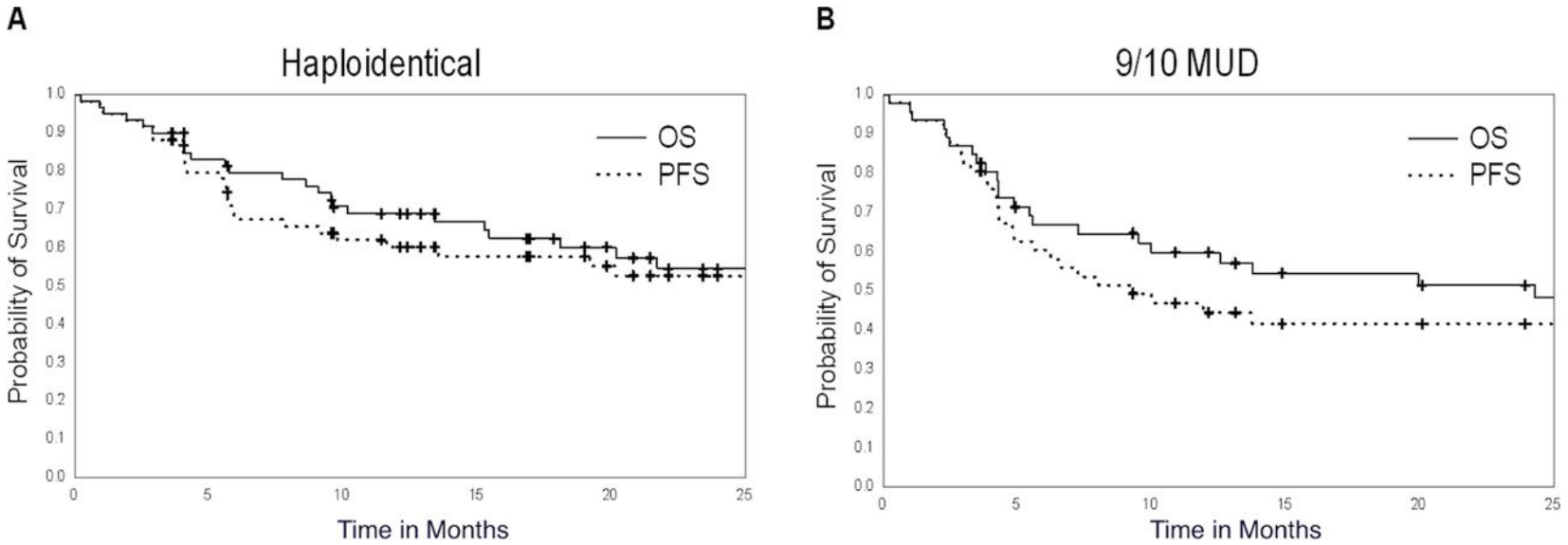

Sameh Gaballa et al. Blood 2015;126:152

	Haplo	MUD 9/10
1-year OS	70%	60%
1- year EFS	60%	47%
Relapse	19%	25%
NRM	21%	31%
aGVHD II-IV	28%	33%
aGVHD III-IV	3%	13%
Extensive cGVHD	13%	10%

Conclusion: This study establishes PTCy, tacrolimus, and mycophenolate as an effective regimen for GVHD prevention in mismatched transplantation using both haploidentical and mismatched unrelated donor sources. Melphalan-based reduced-intensity conditioning is an effective regimen for a broad range of hematologic malignancies. Prospective randomized studies comparing haploidentical and unrelated donor sources are needed.

Sameh Gaballa et al. Blood 2015;126:152

blood

1. Indication

2. Haplo versus donneur alternatif

3. **Quel donneur?**

4. Quelle source de CSH?

HLA Disparities Impact on Outcomes after Unmanipulated Haploidentical Hematopoietic Stem Cells Transplantation (HaploSCT) in Acute Leukemia: A Study from the Acute Leukemia Working Party of the European Group for Blood and Marrow Transplantation (EBMT)

Francesca Lorentino, MD*,[1,2], Fabio Ciceri, MD*,[1,2], Myriam Labopin, MD*,[3,4,2], Zafer Gülbas, MD*,[5], Yener Koc, MD[6], William Arcese, MD[7], Benedetto Bruno, MD PhD*,[8], Johanna Tischer, MD*,[9], Andrea Bacigalupo, MD[10], Didier Blaise[11], Giuseppe Messina, MD*,[12], Martin Bornhäuser, MD*,[13], Katharina Fleischhauer, MD*,[14], Dietrich W. Beelen, MD[15], Annalisa Ruggeri, MD PhD*,[4], Arnon Nagler, MD MSc[16,2], and Mohamad Mohty, MD PhD[3,2,4]

490 patients: (de novo 346 LAM et 144 LAL)

Typage HLA: faible (n=323, 66%) or haute (n=163, 34%) résolution pour HLA-A, -B, -C and -DRB1 loci. Mismatches sont définis au niveau antigénique.

Médiane de suivi: 17 mois (1.3-84)

Médiane âge à la greffe: 44 ans (18-78)

Etat à la greffe: 310 (RC) (63%) (34% RC1, 29% RC2), 180 phase avancée (≥ RC3, rechute ou réfractaire).
Conditionnement: RIC 48% MAC 52%.

Source : CSP 61% Moelle 39%.

Immunosuppression: ATG or Campath 33% post-CY 56% .

HLA D/R: 4 HLAmm sur l'haplotype different (55%), 3 HLAmm (30%), 2 HLAmm (12%), had 1 HLAmm (3%) . En cas de moins de 4 HLAmm, compatibilité pour le locus A (17%), locus B (12%) , locus C (19%) et le locus DRB1 (16%).

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- number of HLAmm on unshared haplotype did not influence outcomes of unmanipulated Haplo-SCT.
- However, a match at HLA-B and HLA-DRB1 loci on unshared haplotype was associated with lower NRM and lower risk of grade 2-4 aGvHD, respectively.

1. Indication
2. Haplo versus donneur alternatif
3. Quel donneur?
4. **Quelle source de CSH?**

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Abstract 3150 Index of Bone Marrow Output and Imbalance of B-Lymphocyte Homeostasis before and after Transplantation Correlate Differently with Graft-Versus-Host Disease and Relapse