Conditionnement à la greffe allogénique : Pourquoi et comment ?

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Disclosures

- **Honoraria:**
  - **Pierre Fabre Medicaments**
  - **Sanofi-Gemzyme**
  - **Jazz Pharmaceuticals**
  - **Keocyt**
  - **Maat Pharma**
  - **Takeda**
  - **Medac**
- **Research Grants:**
  - **Pierre Fabre Medicaments**
  - **Sanofi-Gemzyme**

CONDITIONING REGIMEN IS A MAJOR STEP OF ALLOGENEIC TRANSPLANT

- *The **ideal** preparative regimen for marrow transplantation of patients with malignant diseases should*
  - *Be capable of eradicating malignancy*
  - *Have sufficient immunosuppressive effect … to avoid graft rejection*
  - *Have tolerable morbidity without mortality*
- *The search for an ideal preparative regimen serving all these purposes have been a major focus … over the past 20 years*

NO IDEAL PREPARATIVE REGIMEN CURRENTLY EXISTS

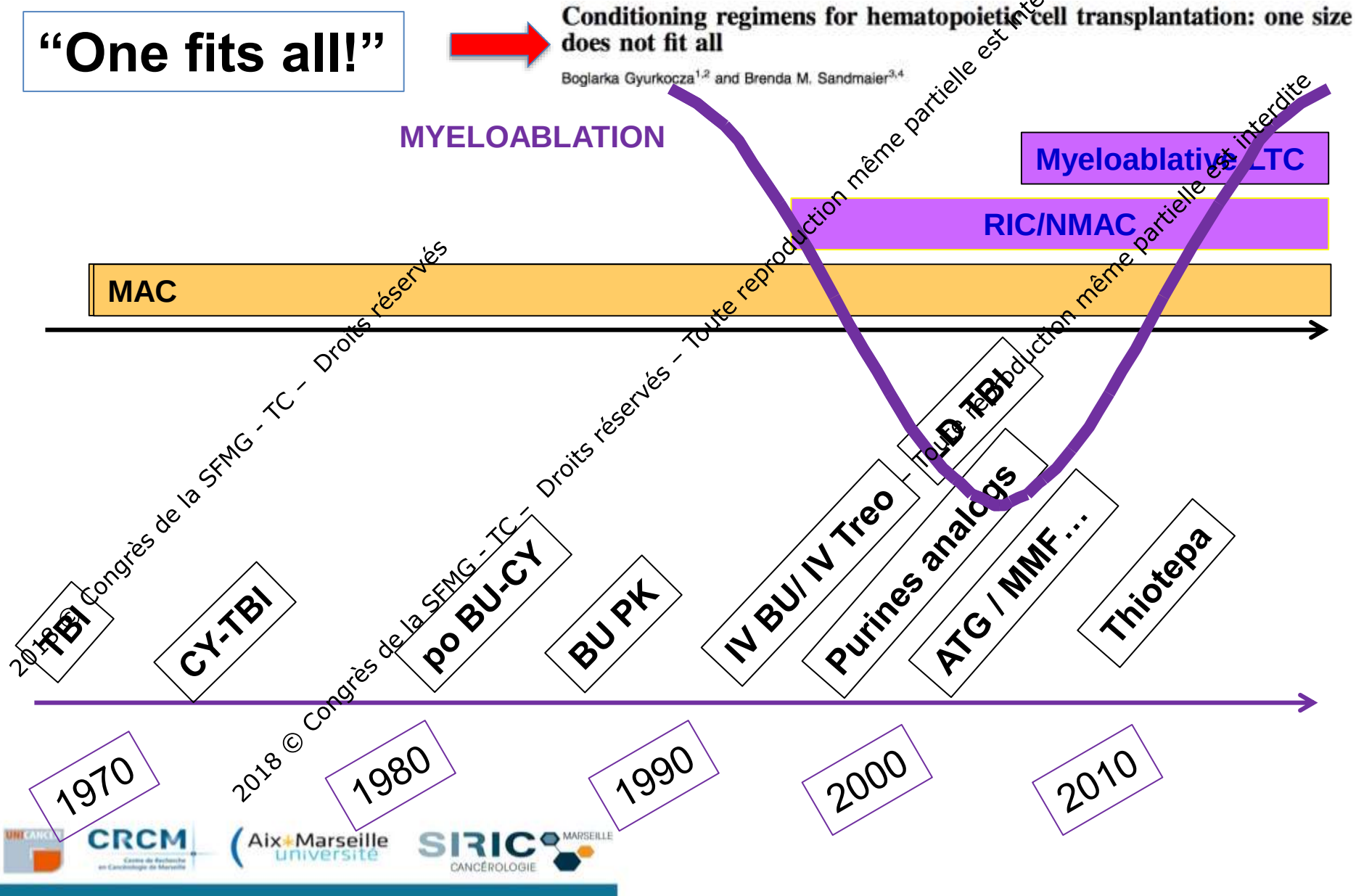
Finn B. Petersen and Scott I. Bearman
Preparative regimens and their toxicity
In Bone Marrow tranplantation
by SJ Forman, KG Blume and ED Thomas, 1994

Conditioning Regimens Evolution

“One fits all!”

Conditioning regimens for hematopoietic cell transplantation: one size does not fit all

Boglarka Gyurkocza[1,2] and Brenda M. Sandmaier[3,4]



Allo-HSCT

Age
- < 45-60 y

Comorbidities
- Sorror < 3

Diseases
- AML CR1
- CML CP

Pre allo:
- Standard Chemotherapy

Donor
- Matched sibling
- Matched unrelated

Graft source
- Bone Marrow

Conditioning
- TBI/Cy
- BU/Cy

Post allo:
- None

Allo-HSCT

Age
- < 45-60 y
- No limit

Comorbidities
- Sorror < 3
- Major comorbidities
- Geriatric assessment

Diseases
- AML CR1
- CML CP
- Non myeloid diseases
- Refractory disease

Pre allo:
- Standard Chemotherapy
- Bridges

Donor
- Matched sibling
- Matched unrelated
- Mismatched donors

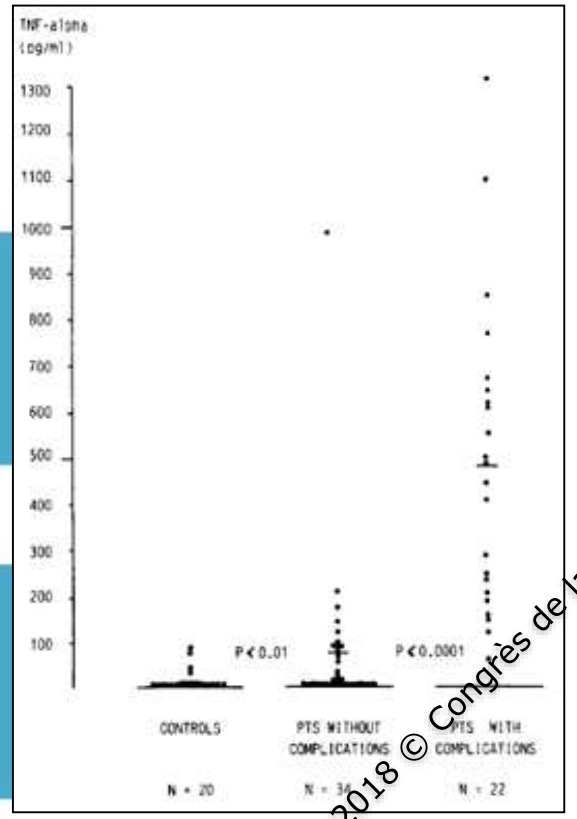
Graft source
- Bone Marrow
- PBSC
- Cord Blood

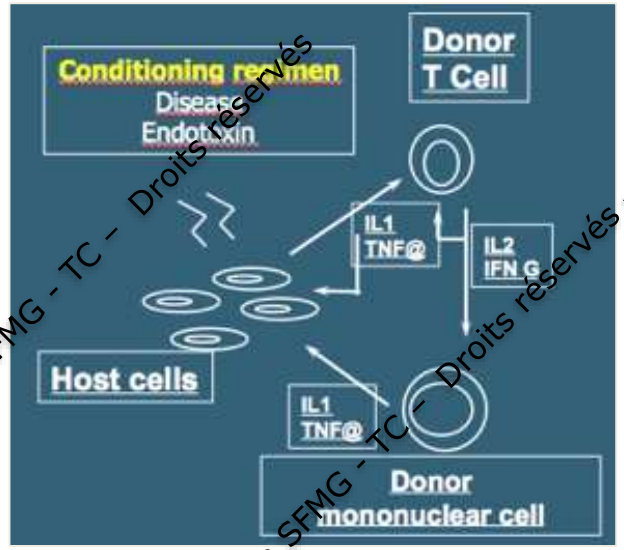
Conditioning
- TBI/Cy
- BU/Cy
- RIC
- NMA
- RTC

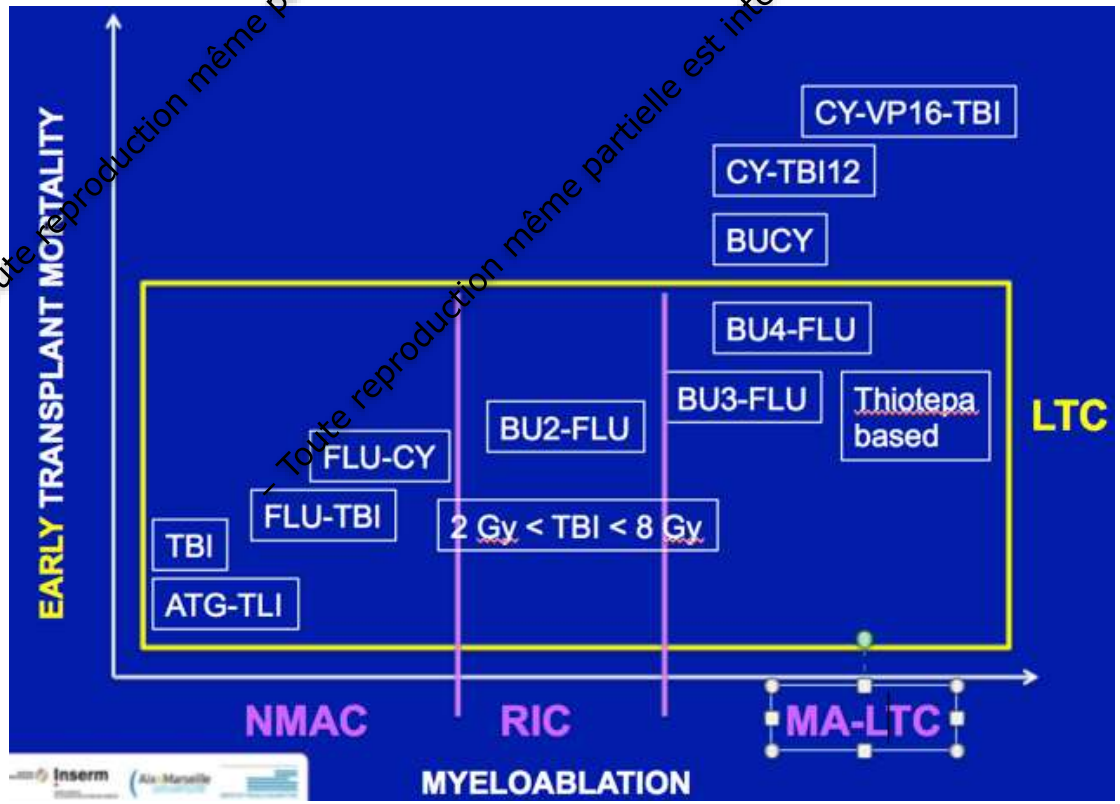
Post allo:
- None
- Chimerism / MRD
- DLI
- New drugs

Results have changed with more thoughtful conditionings

Reduced Intensity and reduced **Toxicity** conditionings





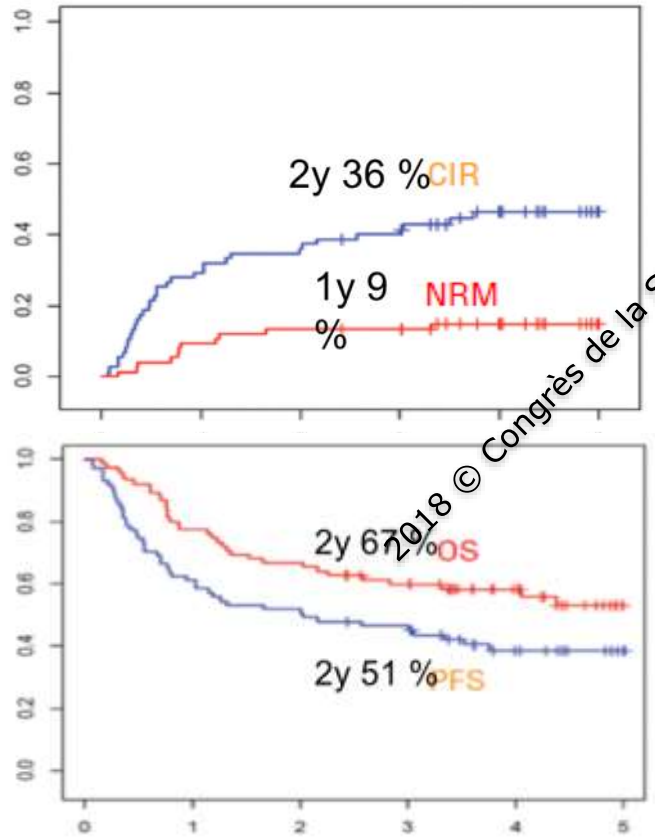


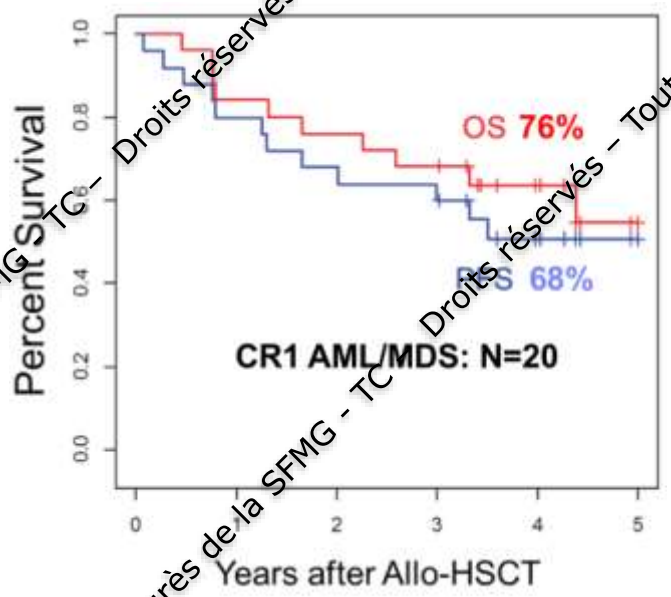
Holler, Blood 1990

Prospective phase II clinical trial
RIC MRD Allo HSCT over the Age of 55 Years

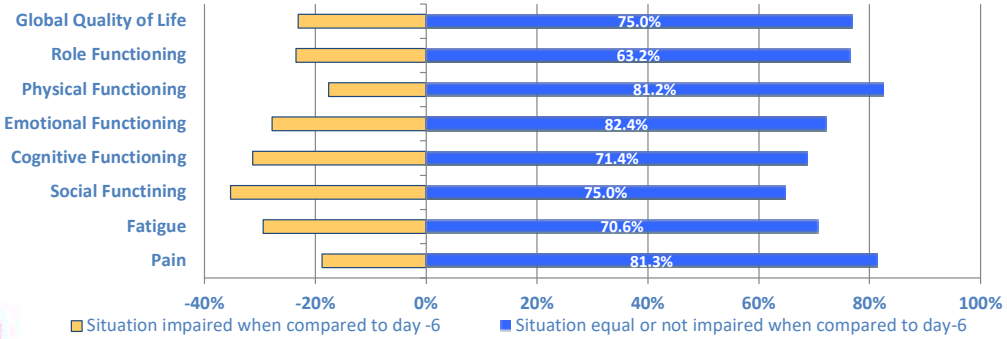
75 patients
Age :60 [55-70]
Malignant Heme H or VH DRI: 17%
Matched Sibling Donor
RIC : Fluda5-Bu2-ATG2

Age	N	NRM	p	OS	p
<60	33	**12%**	0,65	**61%**	0,579
>= 60	42	**17%**		**45%**	





Patients reporting an impaired EORTC score one year after HSCT



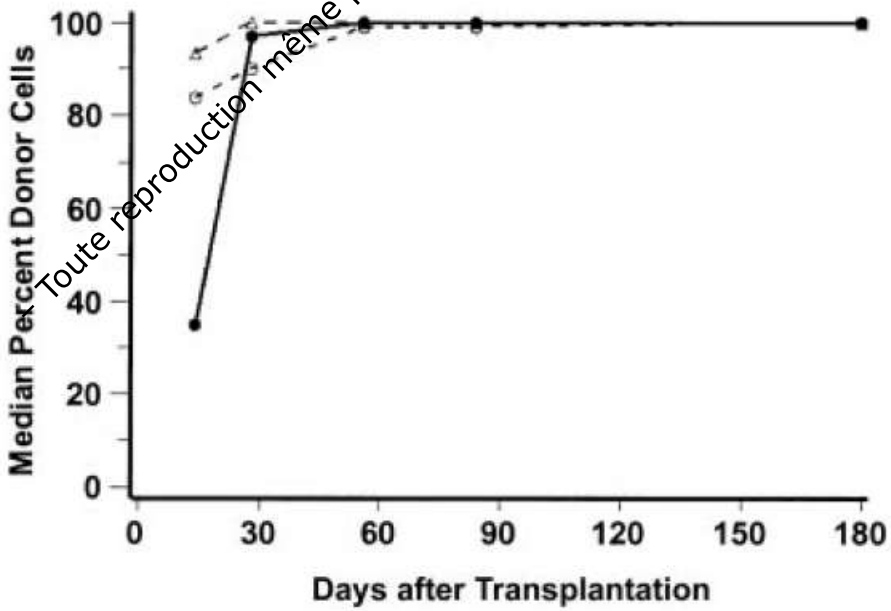
Blaise, Haematologica 2015

Have sufficient immunosuppressive effect … to avoid graft rejection

Non Myeloablative Conditioning

Table 1. Marrow Grafts From DLA-Identical Littermates After Conditioning With Sublethal TBI Delivered at 7 cGy/min or No Conditioning

roup	TBI Dose (cGy)	Postgrafting Immunosuppression	Recipient No.	Sustained Allograft	GVHD		Rejection	Complete Autologous Recovery	Duration of Mixed Hematopoietic Chimerism by $(CA)_n$ Dinucleotide Repeat Marker Studies (weeks after marrow graft)
					Acute	Chronic			
1	200	CSP*	D902	No	—	—	Yes	Yes	4
			D944	No	—	—	Yes	Yes	4
			E026	No	—	—	Yes	Yes	4
			E027	No	—	—	Yes	Yes	4
2	200	MTX†/CSP*	E126	No	—	—	Yes	Yes	7
			E127	No	—	—	Yes	Yes	2
			E156	No	—	—	Yes	Yes	11
			E157	Yes	No	No	No	No	>85
			E200	Yes	No	No	No	No	>60
			E203	Yes	No	No	No	No	>60
3	200	MMF‡/CSP*	E131	Yes	No	No	No	No	>57‖
			E219	Yes	No	No	No	No	>54
			E220	Yes	No	No	No	No	>54
			E066	Yes	No	No	No	No	>56
			E069	No	No	No	Yes	Yes	12
4	100	MMF‡/CSP*	E165	No	—	—	Yes	Yes	12
			E166	No	—	—	Yes	Yes	10
			E202	No	—	—	Yes	Yes	3
			E204	No	—	—	Yes	Yes	3
			E227	No	—	—	Yes	Yes	10
			E228	No	—	—	Yes	Yes	10
5	None	MMF‡/CSP*	E242	No	—	—	Yes	Yes	2
			E244	No	—	—	Yes	Yes	2



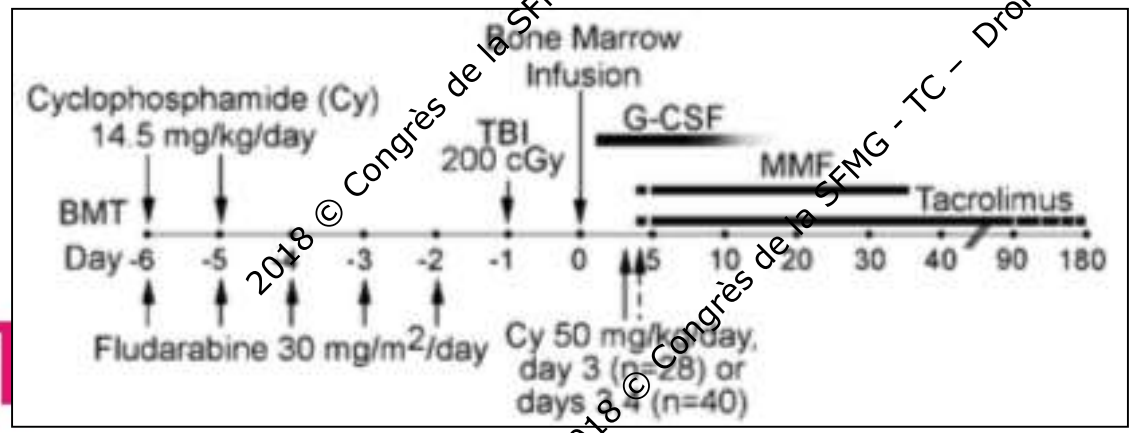
BLOOD, 15 FEBRUARY 2003 VOLUME 101, NUMBER 4

Blood, Vol 89, No 8 (April 15), 1997: pp 3048-305

Have sufficient immunosuppressive effect … to avoid graft rejection

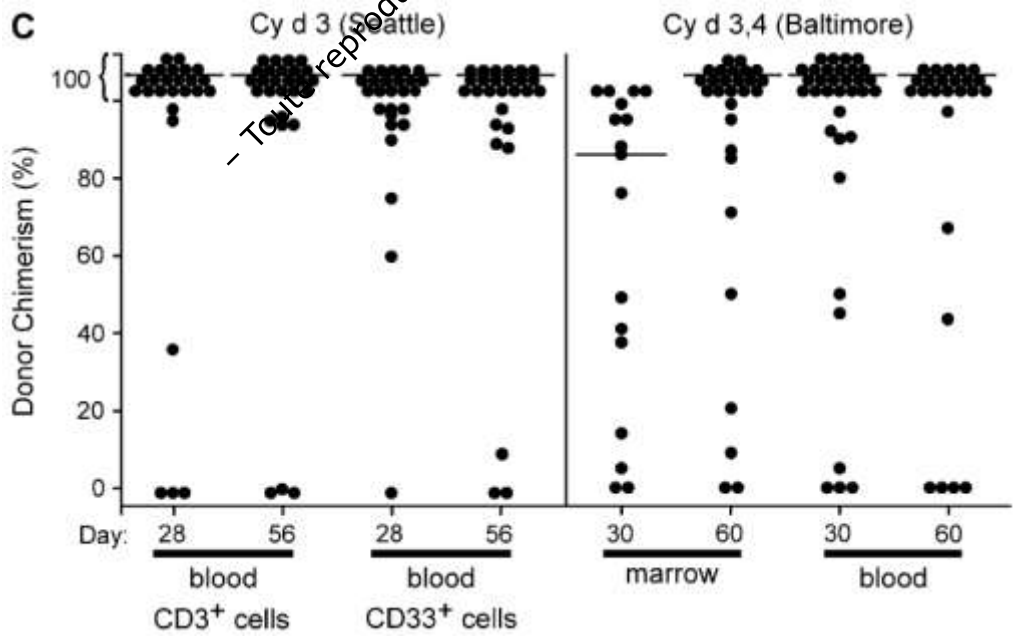
Haplo Donor Transplant (2)

	-10	-9	-8	-7	-6	-5	-4	-3	-2	-1	0
Arac 4g/m²/d	X	X									Primed BM + PBSC
BU 4mg/kg/d			X	X	X						
Cy 1,8 g/M²/d						X	X				
MeCCU 250mg/kg								X			
ATG 20mg/d						X	X	X	X		



Myeloid, platelet recovery and sustained, full donor chimerism were achieved in 249/250 patients

Biol Blood *Marrow* Transplant 15:257-265, 2009



Biol Blood Marrow Transplant 14:641-650 (2008)

Have sufficient immunosuppressive effect … to avoid graft rejection

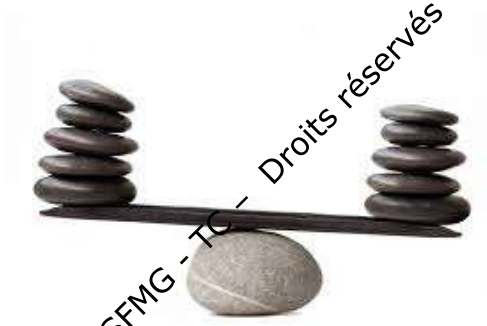
Inadvertent completely HLA-mismatched allogeneic unrelated bone marrow transplant: lessons learned

A male patient, born in 1960, was referred for allogeneic transplantation with a T-cell lymphoma in second CR. A 9/10 allele HLA-matched (HLA-A, -B, -C, -DRB1 and -DQB1) unrelated donor (donor 1) was identified in June 2012. Allogeneic stem cell transplantation was scheduled for September 2012, including arrangements with the donor center (donor center 1). The transplant was canceled because the patient's disease relapsed after which the patient received further treatment and achieved a third CR. A non-myeloablative conditioning regimen transplant was performed in May 2013 with a stem cell graft thought to be from donor 1. One month post transplant, it was recognized that the patient had been transplanted using the wrong donor, due to a query from donor center 1 asking whether their donor (donor 1) was still needed. It was then realized that the patient had been transplanted from donor 2, who turned out to be a complete HLA mismatch (0/10). National and international cooperative transplant centers were consulted, and although the patient was in CR, without evidence of GvHD and fully engrafted with 100% donor chimerism, it was evaluated that this transplantation would

Bone Marrow Transplantation (2016) **51,** 1016–1018; doi:10.1038/bmt.2016.59; published online 14 March 2016

Dose intensity?

Toxicity/Relapse



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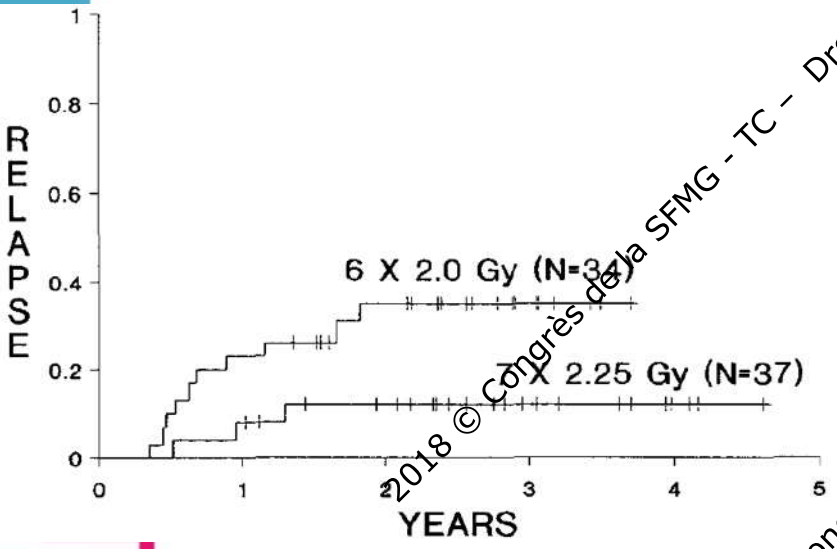
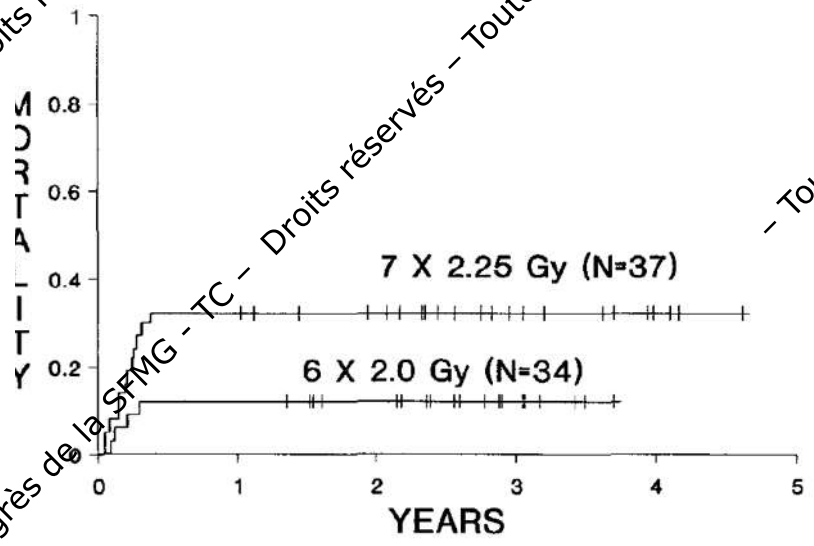
Randomized Evaluation of Dose Intensity

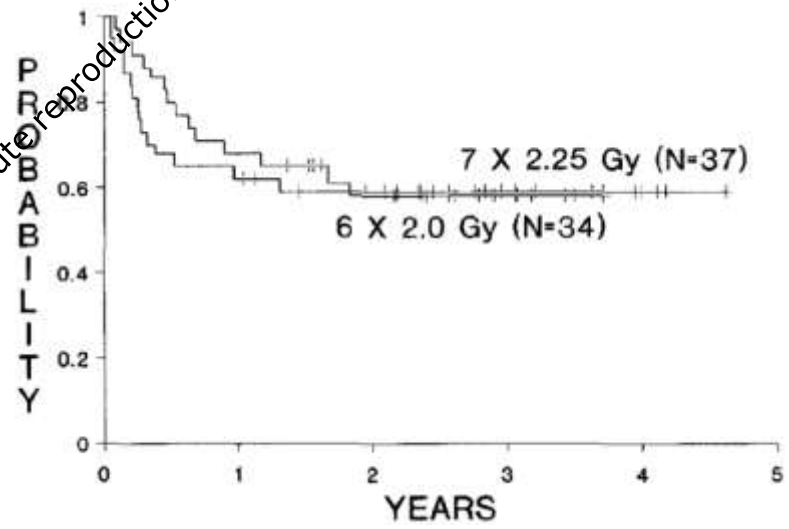
The more intensive, the best?

Allogeneic Marrow Transplantation in Patients With Acute Myeloid Leukemia in First Remission: A Randomized Trial of Two Irradiation Regimens

By Reginald A. Clift, C. Dean Buckner, Frederick R. Appelbaum, Scott I. Beardman, Finn B. Petersen, Lloyd D. Fisher, Claudio Anasetti, Patrick Beatty, W.I. Bensinger, Kristine Doney, Roger C. Hill, George B. McDonald, Paul Martin, Jean Sanders, Jack Singer, Patricia Stewart, Keith M. Sullivan, Robert Witherspoon, Rainer Storb, John A. Hansen, and E. Donnall Thomas





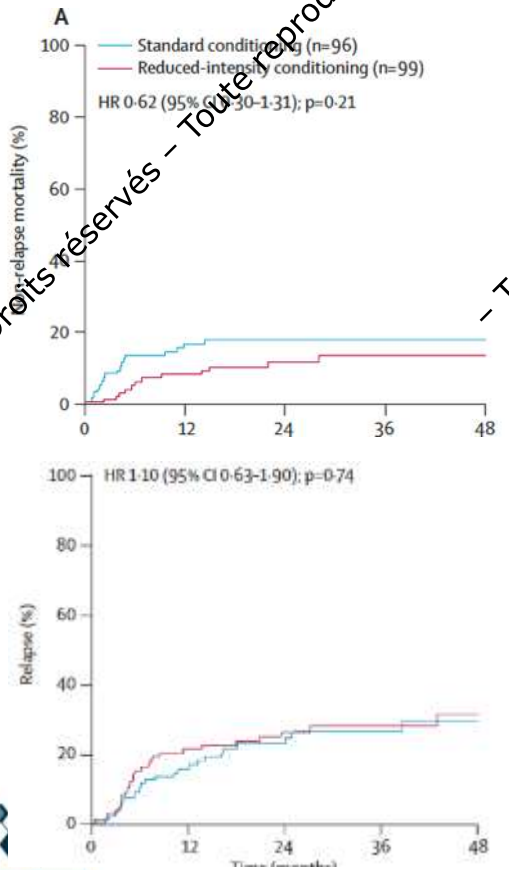


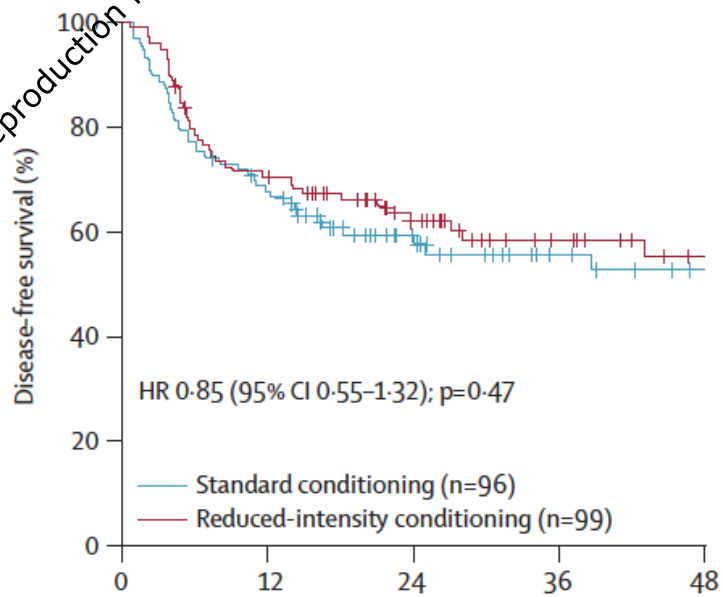
Blood, Vol 76, No 9 (November 1), 1990

Randomized Evaluation of TBI Dose Intensity

RIC versus standard conditioning before allo HSCT in patients with CR1 AML

	Standard conditioning (n=96)	Reduced-intensity conditioning (n=99)
Median age	45 (18–60)	44 (18–60)
Age group		
18–40 years	31 (32%)	35 (35%)
41–60 years	65 (68%)	64 (65%)
Donor		
Matched sibling	58 (60%)	59 (60%)
All alleles matched, unrelated	24 (25%)	28 (28%)
One allele mismatched, unrelated	14 (15%)	12 (12%)





Bornhauser, Lancet Oncology 2012

Randomized Evaluation of Dose Intensity

The less intensive, the best?

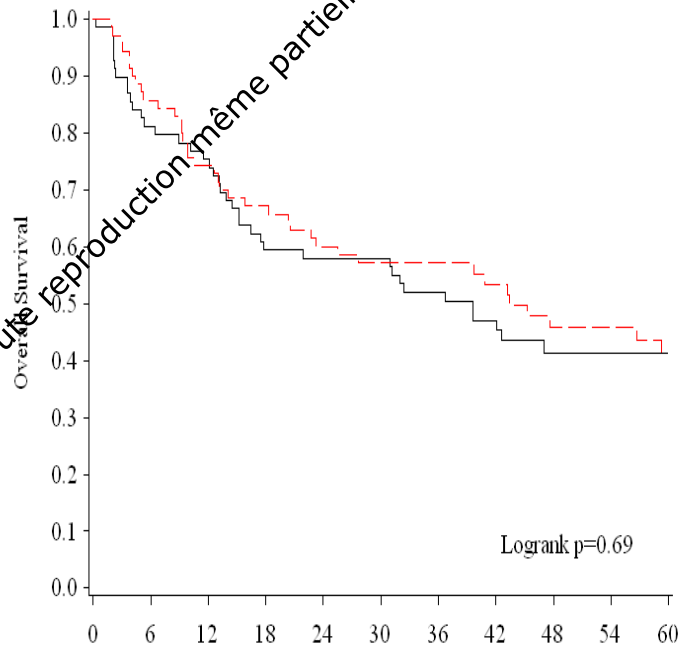
HLA-Matched, Related Allo PBSCT

	Flu-Bu-ATG N=69	Flu-TBI N=70
Age	54 (21-65)	52 (34-65)
- AML/HMY - HLY	37% 63%	27% 73%
- Advanced	63%	65%

Fluda-BU-ATG	D-5	D-4	D-3	D-2	D-1	D0	D+1
Fludarabin: 30 mg/m²	X	X	X	X	X		
Po Busulfan: 4 mg/kg		X					
Thymoglobulin: 2.5 mg/kg			X				
PBSC Transplant						X	
CSA: 3 mg/kg				X	X	X	X→

Fluda-TBI	D-5	D-4	D-3	D-2	D-1	D0	D+1
Fludarabin: 30 mg/m²		X	X	X			
TBI: 2 gy						X	
PBSC Transplant						X	
CSA: 3 mg/kg				X	X		X→
MMF: 2g/day (d1→d+28)							X→

	Flu-Bu-ATG	Flu-TBI
NRM	**38%**	22%
Relapse	27%	**54%**
2-4 aGVHD	**47%**	28%
Ext cGVHD	61%	46%

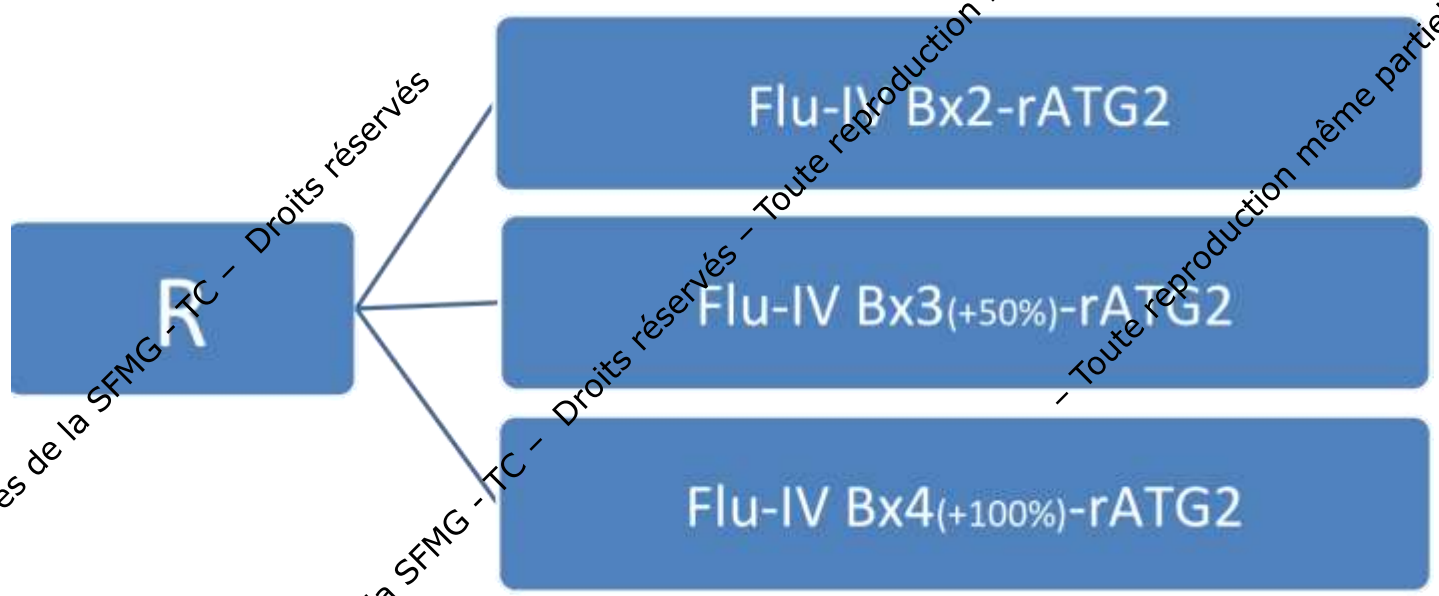


Blaise, D , cancer 2012

Have tolerable morbidity without mortality (2)

Dose Intensity study

NCT 01985061



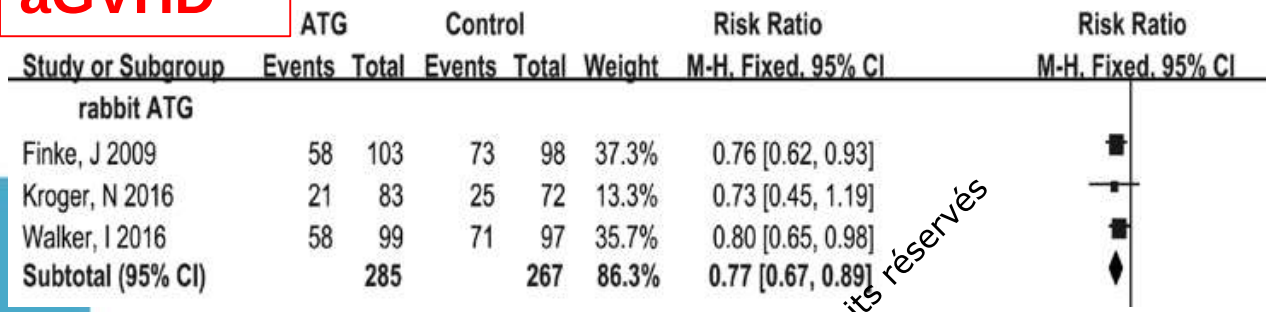
- Eligibility
  - Poor prognosis AML/MDS
  - HLA identical RD or UD
- Primary endpoint : 2 year PFS
- Sample size: 177 patients

- **Quality of life study**
- **Economics**
- Non interventional PK
- BX Pharmacogenomics

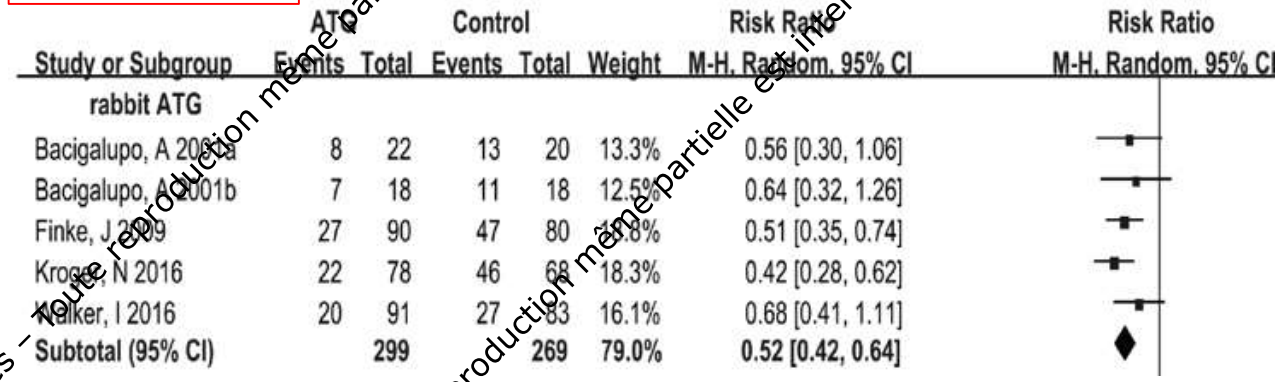
Meta-analysis of the actions of antithymocyte globulin in patients undergoing allogeneic hematopoietic cell transplantation

Jiaojiao Yuan[1,2], Renzhi Pei[2], Wensi Su[1], Junjie Cao[2] and Ying Lu[2]

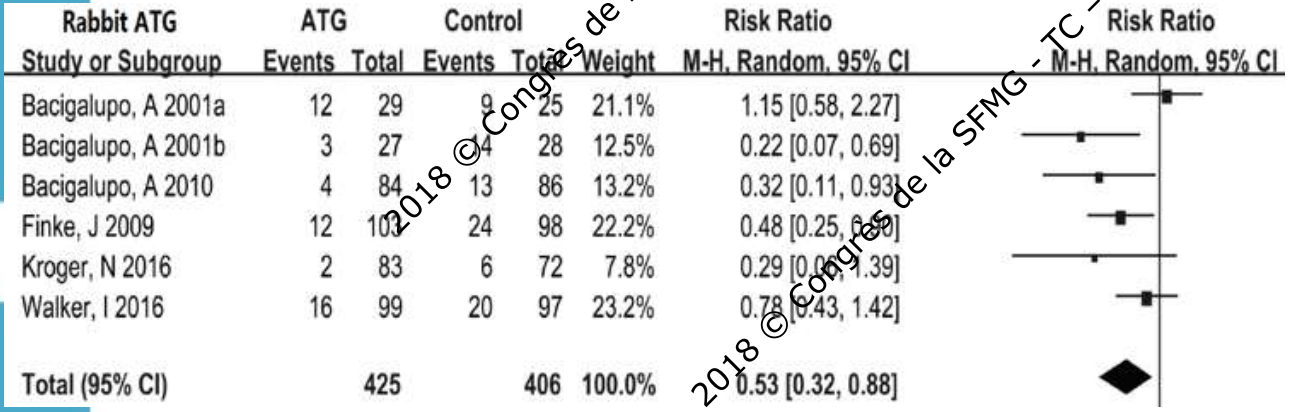
aGVHD



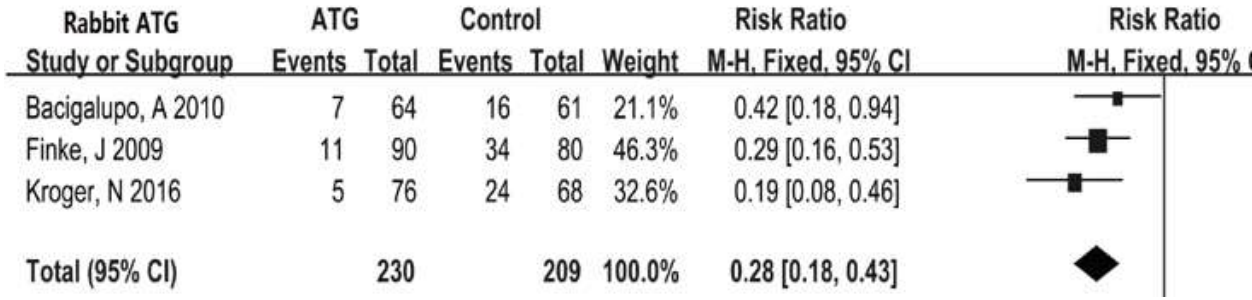
cGVHD



G3-4 aGVHD



Ext cGVHD



Oncotarget, 2017

Meta-analysis of the actions of antithymocyte globulin in patients undergoing allogeneic hematopoietic cell transplantation

Jiaojiao Yuan[1,2], Renzhi Pei[2], Wensi Su[1], Junjie Cao[2] and Ying Lu[2]

Relapse

Rabbit ATG Study or Subgroup	ATG Events	ATG Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Bacigalupo, A 2001a	3	29	3	25	3.7%	0.86 [0.19, 3.90]
Bacigalupo, A 2001b	10	27	5	28	5.6%	2.07 [0.81, 5.28]
Bacigalupo, A 2010	24	84	21	86	23.6%	1.17 [0.71, 1.93]
Finke, J 2009	30	103	23	98	26.8%	1.24 [0.78, 1.98]
Kroger, N 2016	27	83	18	72	21.9%	1.30 [0.78, 2.16]
Walker, I 2016	11	99	16	97	18.4%	0.67 [0.33, 1.38]
Total (95% CI)		**425**		**406**	**100.0%**	**1.17 [0.91, 1.49]**

Risk Ratio M-H, Fixed, 95% CI

100 day Non Relapse Mortality

Rabbit ATG Study or Subgroup	ATG Events	ATG Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Bacigalupo, A 2001a	9	29	5	25	6.4%	1.55 [0.60, 4.03]
Bacigalupo, A 2001b	9	27	11	28	12.9%	0.85 [0.42, 1.72]
Bacigalupo, A 2010	14	84	24	86	28.2%	0.60 [0.33, 1.07]
Champlin, E 2007	5	70	7	60	9.0%	0.61 [0.20, 1.83]
Doney, KC 1981	9	30	12	42	11.9%	1.05 [0.51, 2.17]
Finke, J 2009	12	103	15	98	18.3%	0.76 [0.38, 1.54]
Weiden, P.L 1979	5	29	11	27	13.5%	0.42 [0.17, 1.06]
Total (95% CI)		**372**		**366**	**100.0%**	**0.75 [0.56, 1.00]**

Risk Ratio M-H, Fixed, 95% CI

1 year Overall Survival

Rabbit and horse ATG Study or Subgroup	ATG Events	ATG Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Bacigalupo, A 2001a	17	29	17	25	5.3%	0.86 [0.57, 1.30]
Bacigalupo, A 2001b	11	27	12	28	3.4%	0.95 [0.51, 1.77]
Bacigalupo, A 2010	43	84	42	86	12.1%	1.05 [0.78, 1.43]
Champlin, E 2007	62	70	50	60	15.7%	1.06 [0.92, 1.22]
Doney, KC 1981	16	30	16	42	3.9%	1.40 [0.84, 2.33]
Finke, J 2009	71	103	62	98	18.5%	1.09 [0.89, 1.33]
Kroger, N 2016	68	83	63	72	19.6%	0.94 [0.82, 1.07]
Walker, I 2016	74	99	63	97	18.5%	1.15 [0.96, 1.39]
Weiden, P.L 1979	12	29	10	27	3.0%	1.12 [0.58, 2.15]
Total (95% CI)		**554**		**535**	**100.0%**	**1.06 [0.97, 1.15]**

Risk Ratio M-H, Fixed, 95% CI

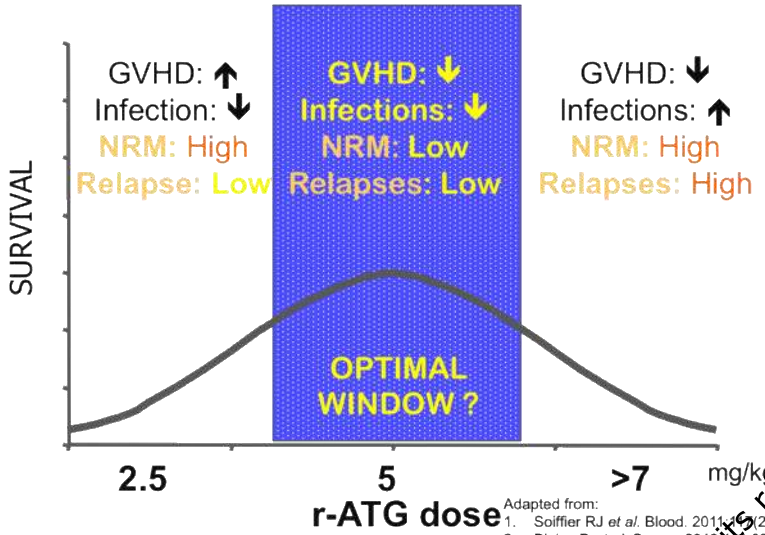
Infections

Study or Subgroup	ATG Events	ATG Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
rabbit ATG						
Kroger, N 2016	48	83	39	72	29.6%	1.07 [0.81, 1.41]
Walker, I 2016	42	99	37	97	24.7%	1.11 [0.79, 1.57]
Subtotal (95% CI)		**182**		**169**	**54.3%**	**1.09 [0.87, 1.35]**

Risk Ratio M-H, Random, 95% CI

Oncotarget, 2017

Importance of r-ATG Dose ?



Adapted from:
1. Soiffier RJ *et al.* Blood. 2011;118(25):6963-70.
2. Blaise D *et al.* Cancer 2012;119:602-11.

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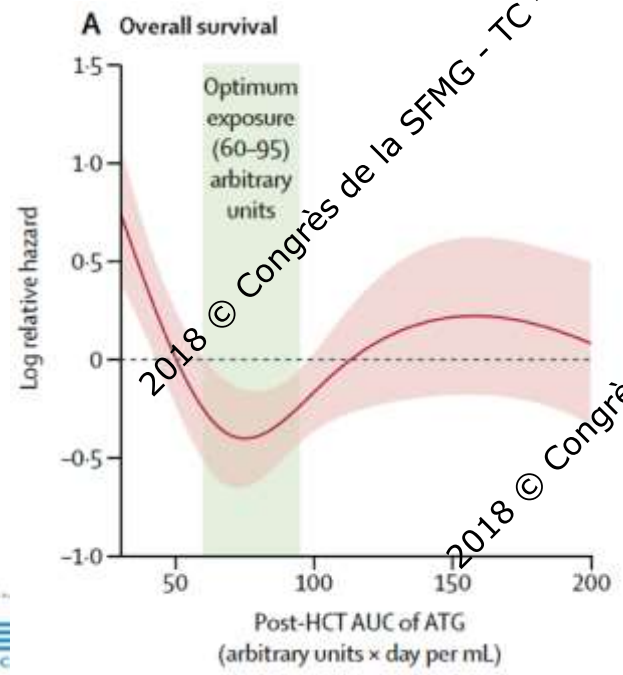

Association between anti-thymocyte globulin exposure and survival outcomes in adult unrelated haemopoietic cell transplantation: a retrospective, pharmacodynamic cohort analysis

Overall survival		
Optimum ATG exposure	1·00 (ref)	..
Below optimum ATG exposure	2·41 (1·15–5·06)	0·020
Above optimum ATG exposure	2·11 (1·04–4·27)	0·038
Event-free survival		
Optimum ATG exposure	1·00 (ref)	..
Below optimum ATG exposure	2·54 (1·29–5·00)	0·0070
Above optimum ATG exposure	1·83 (0·97–3·47)	0·063
Non-relapse mortality		
Optimum ATG exposure	1·00 (ref)	..
Below optimum ATG exposure	4·36 (1·60–11·88)	0·0040
Above optimum ATG exposure	1·64 (0·58–4·62)	0·35
Relapse mortality		
Optimum ATG exposure	1·00 (ref)	..
Below optimum ATG exposure	1·45 (0·55–3·83)	0·46
Above optimum ATG exposure	2·66 (1·12–6·31)	0·027
Relapse incidence		
Optimum ATG exposure	1·00 (ref)	..
Below optimum ATG exposure	1·28 (0·57–2·86)	0·55
Above optimum ATG exposure	1·79 (0·89–3·61)	0·11

Admiraal R *et al*. Lancet Hematol. 2017

New drugs?
or new ways to use old drugs?

- Alkylating agents
  - Busulfan
  - Treosulfan
  - Thiotepa
- Immunosuppressive agents
  - Fludarabine
  - Other purin analogs

“There is nothing new under the sun but there are lots of old things we don’t know.”
Ambrose Bierce, The Devil’s Dictionary

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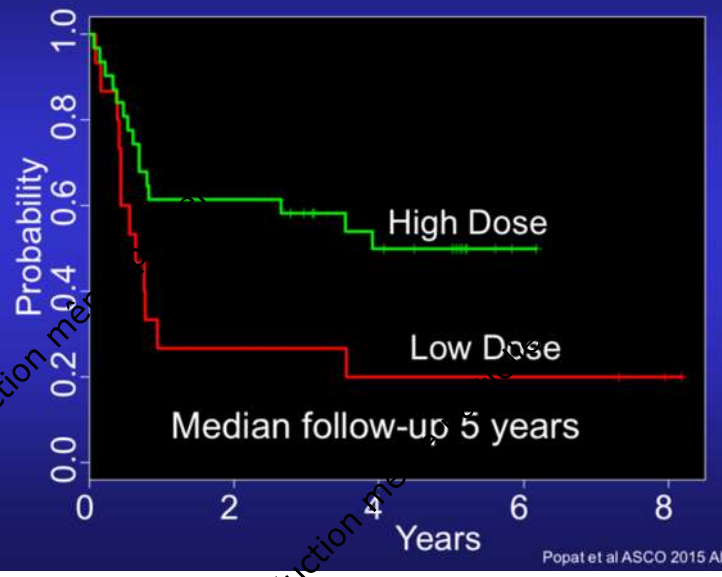
How do you improve outcomes?

Can you intensify the conditioning regimen without increasing toxicity and mortality?

Myelofibrosis : PK Guided Higher Dose Busulfan (Course AUC 16,000) Improves EFS



Popat et al ASCO 2015 Abstr. 7008

Fludarabine-Busulfan
Randomized study of busulfan dosing

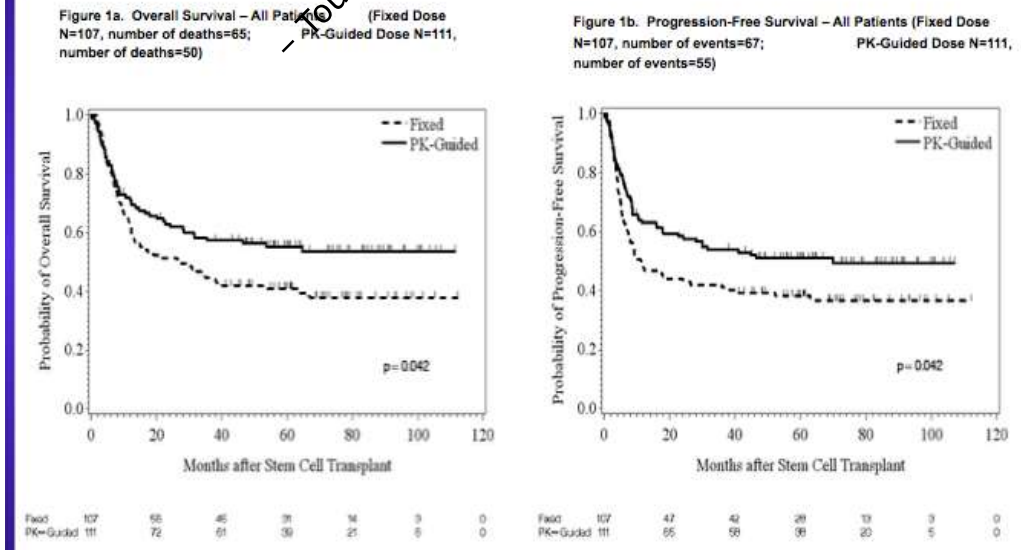
AML/MDS

→ PK Adjusted dose AUC 6000 µMol-min

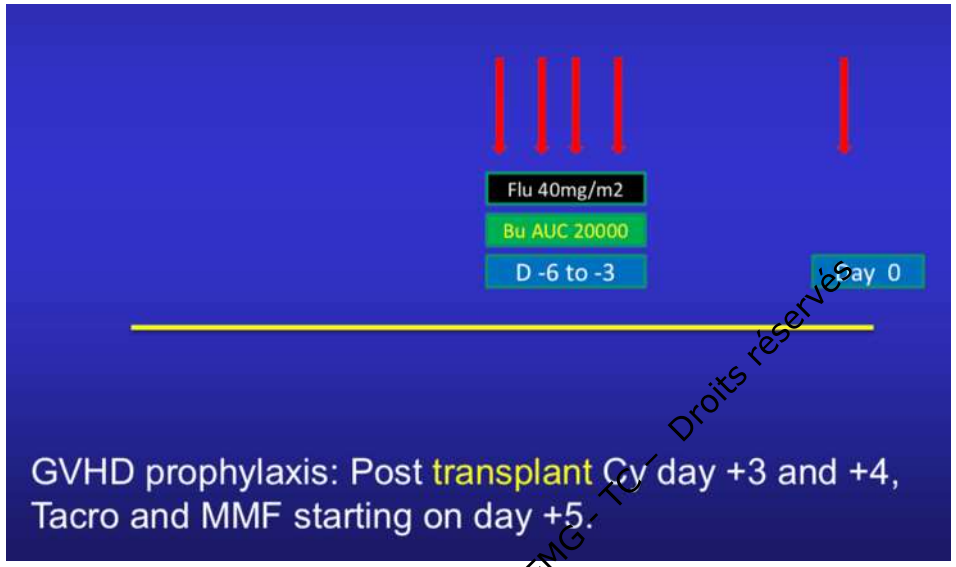
→ Fixed dose 130 mg/m², results in an average AUC ~5000 µMol-min

The dose adjusted group will have an average dose escalation of ~20% and a consistent AUC at that level.

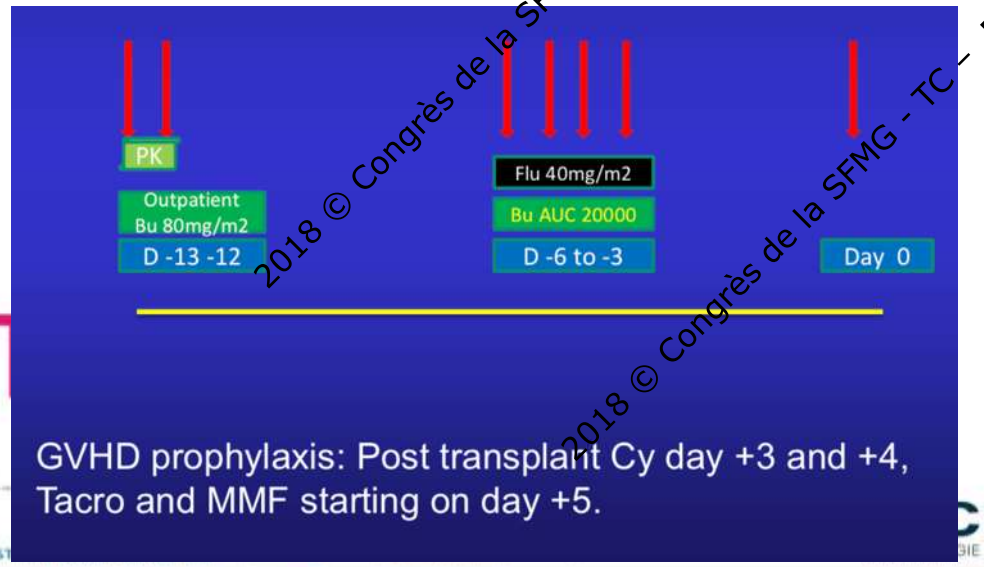
OS and PFS after PK-guided and Fixed dose Bu in AML/MDS



Myeloablative Timed Sequential Busulfan Conditioning



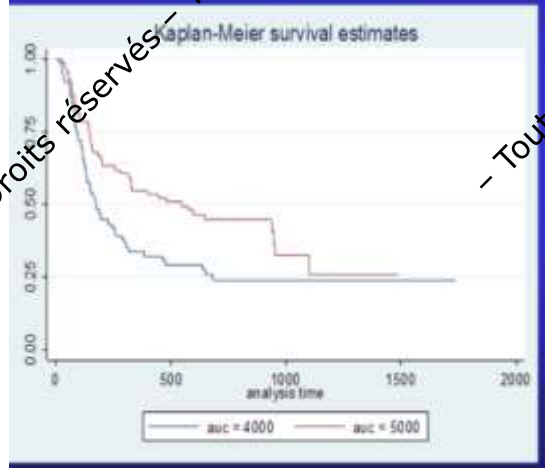
GVHD prophylaxis: Post transplant Cy day +3 and +4, Tacro and MMF starting on day +5.



GVHD prophylaxis: Post transplant Cy day +3 and +4, Tacro and MMF starting on day +5.

Better Survival with Timed Sequential Busulfan

Progression Free Survival



Outcomes at 2 Years

	Standard Cohort Median age 66		TS Cohort Median age 65		TS vs STD		
	N=78		N=84		HR	95% CI	P
OS	31%	(20-42)	51%	(39-62)	0.6	0.3-0.9	0.01
PFS	24%	(15-34)	45%	(33-55)	0.6	0.4-0.8	0.004
Progress	59%	(48-71)	34%	(25-46)	0.5	0.3-0.8	0.003
D100 NRM	3%	(1-10)	5%	(2-12)	1.9	0.3-10	0.5
2 yr NRM	15%	(9-26)	21%	(14-33)	1.4	0.7-3	0.3

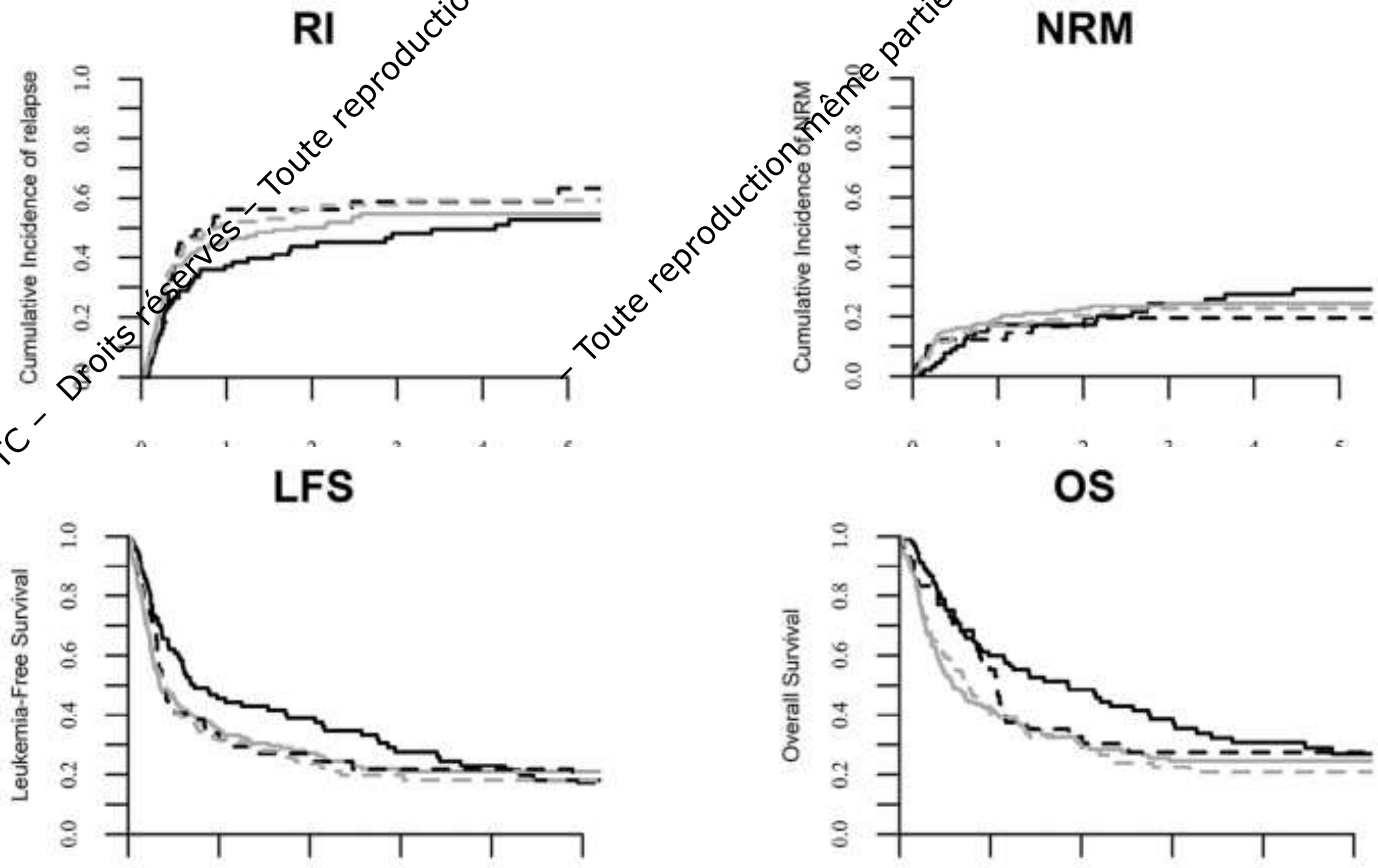
Popat et al ASCO 2017

Intravenous Busulfan Compared with Treosulfan-Based Conditioning for Allogeneic Stem Cell Transplantation in Acute Myeloid Leukemia: A Study on Behalf of the Acute Leukemia Working Party of European Society for Blood and Marrow Transplantation

Avichai Shimoni [1,*], Myriam Labopin [2], Bipin Savani [3], Rose-Marie Hamladji [4], Dietrich Beelen [5], Ghulam Mufti [6], Gerard Socié [7], Jeremy Delage [8], Didier Blaise [9], Patrice Chevallier [10], Edouard Forcade [11], Eric Deconinck [12], Mohamad Mohty [13], Arnon Nagler [1,2]

Multivariate Analysis of Factors Predicting Acute and Chronic GVHD

	Acute GVHD Grades II-IV		Chronic GVHD	
	HR (95% CI)	*P*	HR (96% CI)	*P*
Conditioning				
FB4	1		1	
FB2	.78 (.64-.95)	.01	.89 (.74-1.06)	.19
FT14	.63 (.48-.83)	.0009	1.06 (.86-1.30)	.61
FT12	.56 (.37-.84)	.005	.65 (.46-.91)	.01
Age per 10 yr	1.08 (1.00-1.16)	.05	1.05 (.98-1.12)	.15
Gender, female	.96 (.81-1.14)	.63	1.02 (.81-1.15)	.69
Disease status				
CR1	1		1	
CR2/3	1.17 (.95-1.44)	.14	1.10 (.91-1.32)	.33
Active disease	1.13 (.90-1.40)	.28	1.13 (.91-1.40)	.27
Secondary AML	1.13 (.93-1.37)	.21	.97 (.81-1.15)	.69
Donor, unrelated	1.77 (1.45-2.15)	<.0001	1.22 (1.04-1.44)	.02
F → M	1.01 (.81-1.27)	.92	1.31 (1.09-1.58)	.004
Stem cell source, PBSC	1.13 (.87-1.48)	.36	1.33 (1.07-1.66)	.01
Patient CMV+	1.16 (.96-1.41)	.13	1.09 (.93-1.28)	.30
Donor CMV+	1.05 (.88-1.25)	.59	1.08 (.93-1.25)	.34
In vivo TCD	.74 (.60-.90)	.003	.56 (.48-.66)	<.0001
Year of SCT	1.00 (.97-1.03)	.98	.97 (.94-.99)	.02



Why include TEPADINA® in a preparative regimen prior to HSCT?

- The early stages of clinical development showed the **efficacy of thiotepa against various neoplastic diseases** such as ***leukemia, lymphoma, CNS*** tumours, breast cancer and ovarian cancer

- Excellent ***myeloablative and Immunosuppressive*** activities

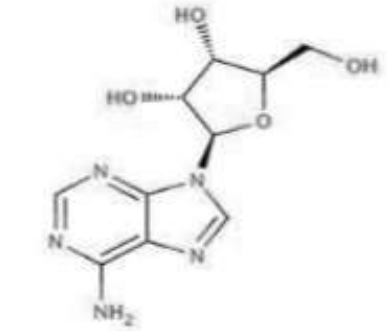
- ***Low non-hemopoietic toxicity*** and ***lack of cumulative toxicity*** with TBI, busulfan, treosulfan, cyclophosphamide or fludarabine

- Doses could be ***escalated up to 15 mg/kg*** without triggering significant extra-hematological toxicity

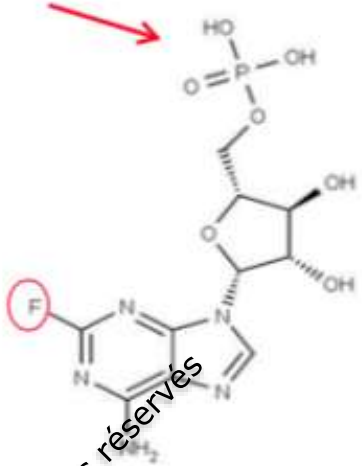
- Penetration of blood-brain barrier and blood-cerebral spinal fluid ***avoiding neurotoxicity***

- Thiotepa can be used in a **wide spectrum of *patients and diseases*** from paediatric to elderly!

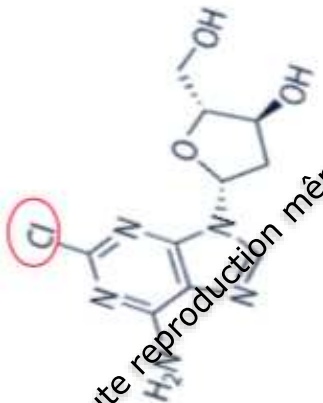
Nucleoside Analogs (NAs)



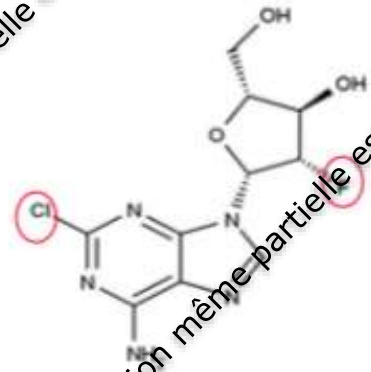
Adenosine



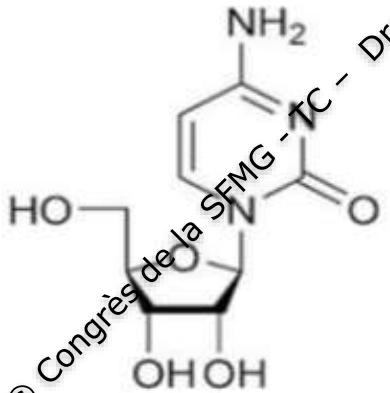
Fludarabine



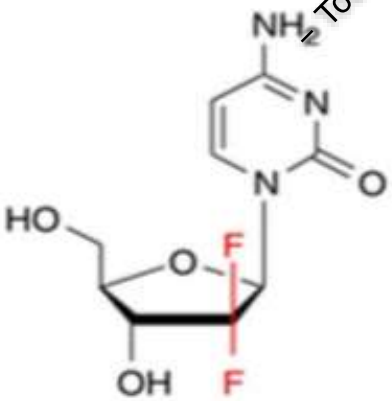
Cladribine



Clofarabine



Cytidine



Gemcitabine

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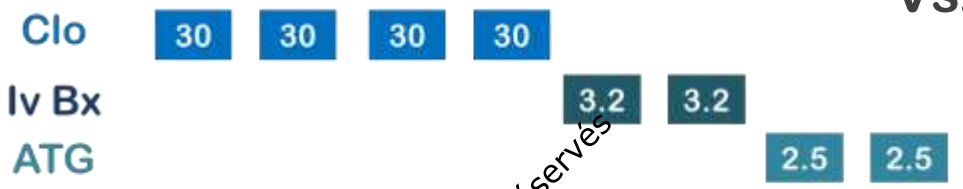
RIC Clo-Bu-ATG vs. Flu-Bu-ATG AML / MDS

Retrospective Registry Study



Vs.

	CloBA	FBA
N	39	316
AML	62%	79%
CR1	69%	72%
MUD	56%	66%

	CloBA	FBA
2-y NRM	26%	16%
2-y CIR	26%	45%
2-y PFS	63%	39%
2-y OS	76%	47%

Chevallier Cancer Medicine 2016

MAC Clo + Flu + Bu for advanced diseases

Prospective Randomized Phase II Trial

R

Clo	10	10	10	10
Flu	30	30	30	30
Iv Bx	PK	PK	PK	PK
Clo	20	20	20	20
Flu	20	20	20	20
Iv Bx	PK	PK	PK	PK
Clo	30	30	30	30
Flu	10	10	10	10
Iv Bx	PK	PK	PK	PK
Clo	40	40	40	40
Flu	0	0	0	0
Iv Bx	PK	PK	PK	PK

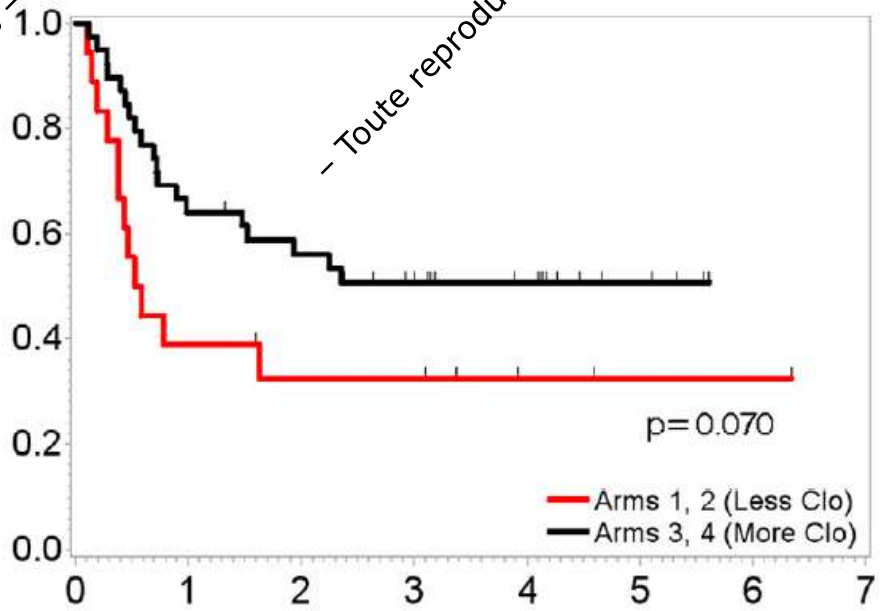
N = 70

AML 81%

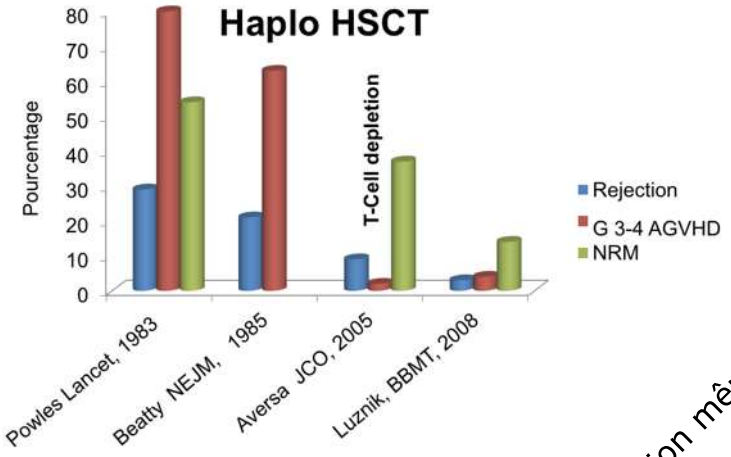
Age 46 (6-59)

Active disease 81%

MUD 59%



Alatrash BBMT 2016



Present T replete Haplo HSCT

MAC + HD ATG + Primed BM + PBSC
Beijing University

	-10	-9	-8	-7	-6	-5	-4	-3	-2	-1	0
Arac 4g/m²/d	X	X									
BU 4mg/kg/d			X	X	X						
Cy 1,8 g/M²/d						X	X				
MeCCU 250mg/kg								X			
ATG 20mg/d						X	X	X	X		
Primed BM + PBSC											

Huang et al, BMT, 2006

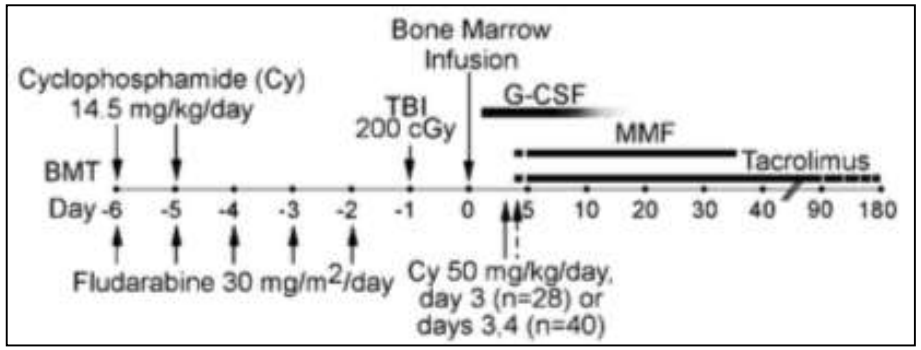
RIC/MAC + HD ATG + PBSC
Korea

	-9	-8	-7	-6	-5	-4	-3	-2	-1	0
TBI 200cgy x2	X	X								
Fludarabin 30mg/m²			X	X	X	X	X			
Bu: 3,2mg/kg				X	X					
Thymo: 1,25 mg/kg						X	X	X	X	

	-9	-8	-7	-6	-5	-4	-3	-2	-1	0
(TBI 200cgy x2)	(X)	(X)								
Fludarabin 30mg/m²			X	X	X	X	X	X		
Bu: 3,2mg/kg			X	X						
Thymo: 3 mg/kg						X	X	X	X	

Lee et al, Blood, 2011; Shin et al, BBMT, 2015
Yahng et al, BBMT, 2015

NMAC + BM + HD PTCy
Johns Hopkins



Luznick et al, BBMT, 2008

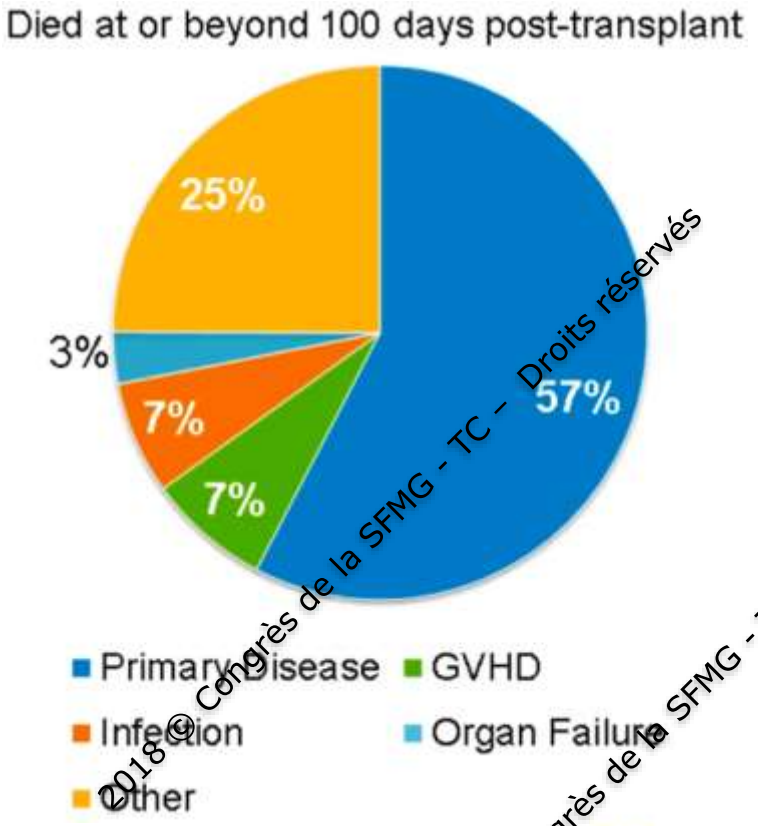
Haploidentical transplant with posttransplant cyclophosphamide vs matched unrelated donor transplant for acute myeloid leukemia

	MAC N=104	RIC N=88
G2-4 aGVHD	16%	19%
3 y cGVHD	30%	34%
NRM	**14%**	**9%**
Relapse	**44%**	**58%**
3 y OS	45%	46%

	MAC N=104	RIC N=88
Age > 51	**42%**	**78%**
PS < 80%	48%	26%
Disease status		
CR1	46%	46%
CR2	22%	35%
Ref	**32%**	**16%**
HR DRI	**32%**	**18%**
Adverse Cytog	**22%**	**11%**
PBSC	18%	13%
2011-2012	**76%**	**45%**
Fup	**30mths**	**39mths**

Ciurea, Blood, 2015

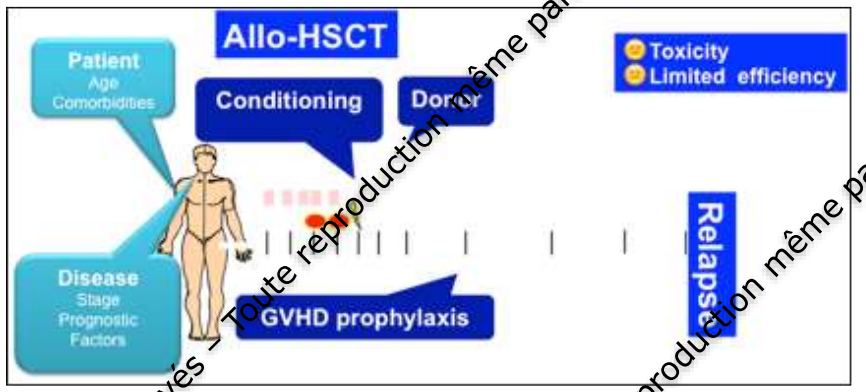
Be capable of eradicating malignancy



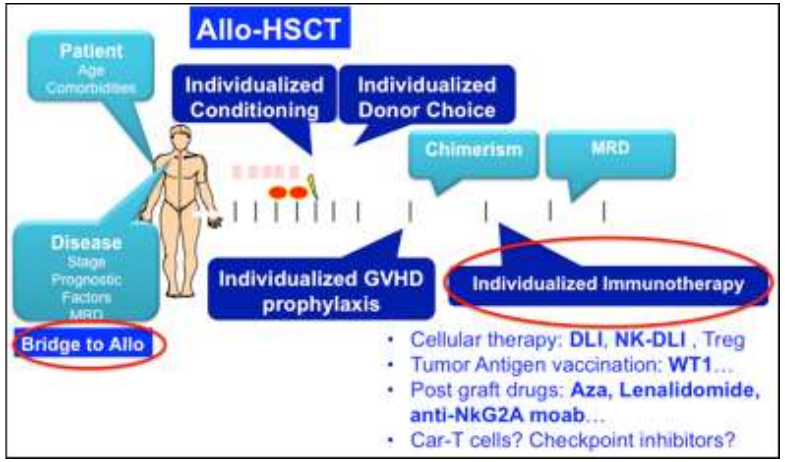
Current uses and outcomes of HCT
2016 Summary Slides

CIBMTR

Allogeneic Transplantation



Allogeneic Immunotherapy



CONDITIONING REGIMEN IS A MAJOR STEP OF ALLOGENEIC TRANSPLANT

- *The **ideal** preparative regimen for marrow transplantation of patients with malignant diseases should*
  - ~~*Be capable of eradicating malignancy*~~
  - Be capable to avoid rapid disease evolution
  - Have sufficient immunosuppressive effect … to avoid graft rejection
  - ~~*Have tolerable morbidity without mortality*~~
  - Has the lowest mortality **and**
  - Does not cause organ toxicity or severe GVHD foreclosing secondary immune intervention

A last question!

Do we need conditioning for allogeneic immunotherapy?

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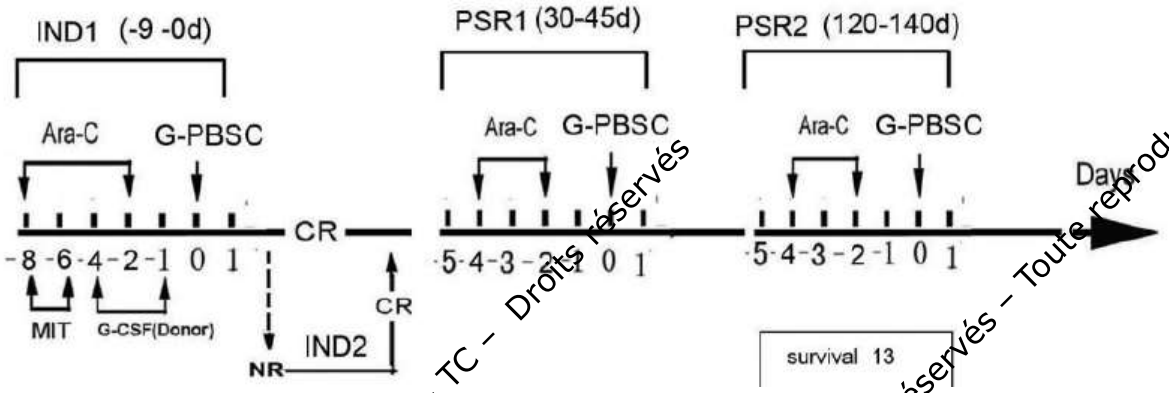
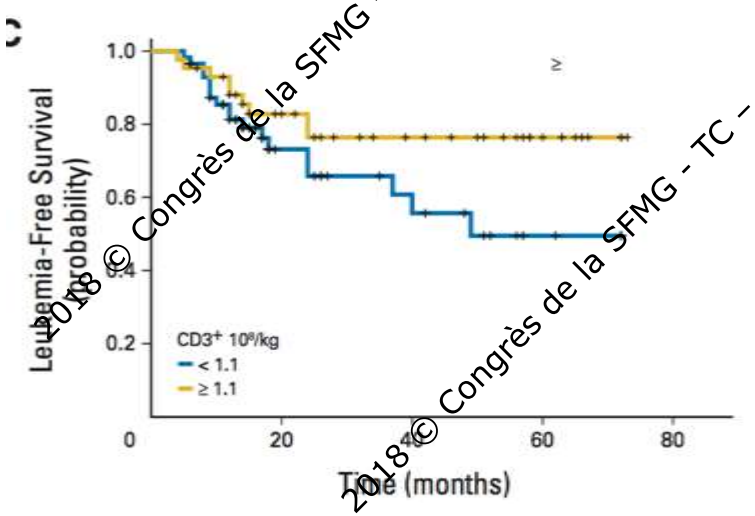
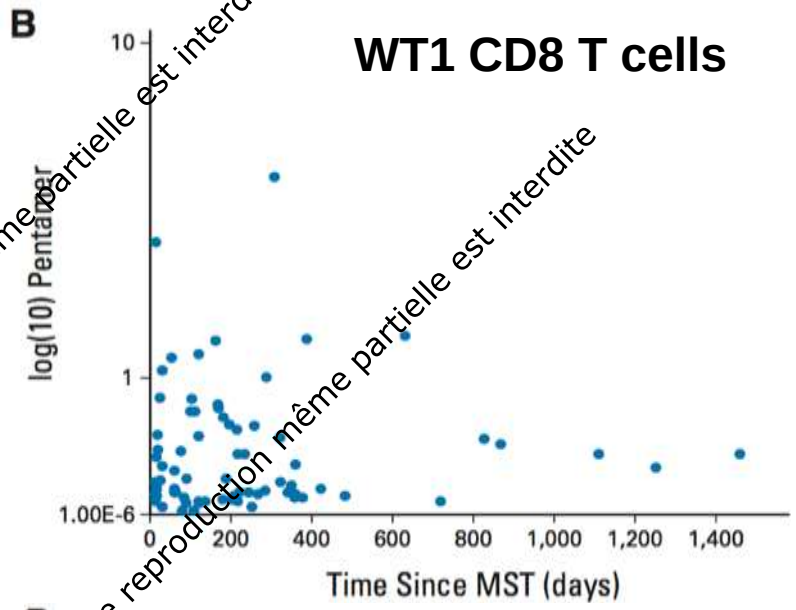
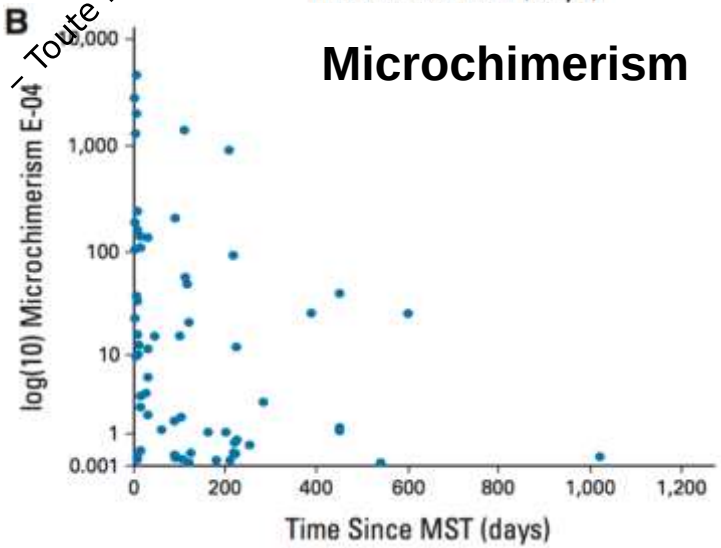
HLA-Mismatched Stem-Cell Microtransplantation As Postremission Therapy for Acute Myeloid Leukemia: Long-Term Follow-Up

Mei Guo, Kai-Xun Hu, Guang-Xian Liu, Chang-Lin Yu, Jian-Hui Qiao, Qi-Yun Sun, Jun-Xiao Qiao, Zheng Dong, Wan-Jun Sun, Xue-Dong Sun, Hong-Li Zuo, Qiu-Hong Man, Zhi-Qing Liu, Tie-Qiang Liu, Hong-Xia Zhao, Ya-Jing Huang, Li Wei, Bing Liu, Juan Wang, Xu-Liang Shen, and Hui-Sheng Ai









J Clin Oncol 30:4084-4090. © 2012