

Controversies in AML

ANCONA • 16 GIUGNO 2023

SEEPOR HOTEL

Will PTCy replace ATG as GVHD prophylaxis in unrelated donor HSCT for AML?

YES

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No COI to disclose



Background: GVHD prophylaxis with ATG

- GVHD is associated with considerable morbidity and mortality related to allo-HSCT
- In vivo TCD with ATG has been shown to reduce the incidence of GVHD, particularly in its chronic form and when using PBSC
- ATG represents the standard GVHD prophylaxis in EU in HLA-id sib allo-HSCT or UD allo-HSCT

Table 4. Proposed indications for immunoregulation with ATG in patients given PBSC from allogeneic donors.

	Recommendation for ATG	Dose and timing of ATG
Myeloablative PBSCT from matched sibling donors ⁵⁶	standard of care	ATG-F 10 mg/kg/day on days -3, -2 and -1.
Myeloablative PBSCT from HLA-matched unrelated donors ^{56,68,67}	standard of care	ATG-F 20 mg/kg/day on days -3, -2 and -1*. ATG-T 0.5 mg/kg on day -2 and 2 mg/kg on days -1 and +1.
RIC-PBSCT fludarabine-busulfan ⁶⁸	recommended	ATG-T 2.5 mg/kg/day on days -2 and -1.
Non-myeloablative PBSCT	developmental	/
HLA-haplo-identical stem cell transplantation (Beijing approach) ⁶⁸	standard of care	ATG-T 2.5 mg/kg/day from days -5 to -2.

* some centers use smaller doses such as 15 mg/kg total dose

Baron F et al. Haematologica 2017

ATG in GVHD prophylaxis

Table 1. Summary of 3 randomized trials

	GITMO ^{6,7}		Finke ^{8,9}		Kröger ¹⁰		Total		RR	P
	ATG	noATG	ATG	noATG	ATG	noATG	ATG	noATG		
Patients, n	56	53	103	98	83	72	242	223	–	–
aGVHD IHV, %	50%	70%	33%	51%	11%	18%	31%	46%	1.47	.001
aGVHD IIHV, %	23%	43%	11%	24%	2%	8%	12%	25%	2.08	.0003
cGVHD, %	37%	60%	26%	50%	22%	46%	28%	52%	1.83	.00001
ext cGVHD, %	15%	41%	12%	45%	5%	24%	11%	37%	3.43	.00001
NRM, %	39%	47%	19%	33%	14%	12%	24%	31%	1.27	.1
Relapse, %	23%	21%	33%	28%	32%	25%	29%	25%	0.84	.2
Survival, %	55%	56%	55%	43%	74%	77%	61%	59%	1.04	.6

ext, extensive; GITMO, Italian Cooperative Transplant Group; NRM, non-relapse mortality; RR, relative risk of patients not receiving ATG as compared with ATG.

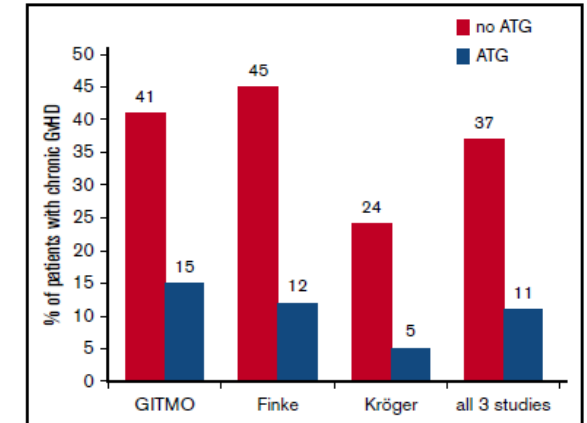


Figure 1. Percentage of patients with severe cGVHD in 3 randomized trials. (GITMO,^{6,7} Finke,^{8,9} Kröger,¹⁰ and combined data [total] are shown).

ARTICLES | VOLUME 17, ISSUE 2, P164-173, FEBRUARY 2016

Pretreatment with anti-thymocyte globulin versus no anti-thymocyte globulin in patients with haematological malignancies undergoing haemopoietic cell transplantation from unrelated donors: a randomised, controlled, open-label, phase 3, multicentre trial

Prof Irwin Walker, MBBS • Tony Panzarella, MSc • Prof Stephen Couban, MD • Prof Felix Couture, MD • Prof Gerald Devins, PhD • Mohamed Elemery, MD • Prof Geneviève Gallagher, MD • Holly Kerr, RN • John Kuruvilla, MD • Prof Stephanie J Lee, MD • John Moore, MD • Prof Thomas Nevill, MD • Gizelle Popradi, MD • Prof Jean Roy, MD • Kirk R Schultz, MD • David Szwajcer, MD • Prof Cynthia Toze, MD • Ronan Foley, MD • on behalf of the Canadian Blood and Marrow Transplant Group • [Show less](#)

Bacigalupo A. Blood Adv 2017

ATG for GVHD prophylaxis: counterpoints

- Not all ATG formulations are the same → interpatient variability and lack of head-to-head comparative studies
- Delayed immune reconstitution¹
- Higher infectious risk, EBV reactivation and PTLD^{2,3}
- Higher relapse incidence⁴

¹Mohty M et al. *Bone Marrow Transplant* 2000

²Bacigalupo A et al. *Blood* 2001

³Walker I et al. *Lancet Oncol* 2016

⁴Soiffer RJ et al. *Blood* 2011



The PTCy “revolution”

- In vivo T-cell depletion with the use of PTCy initially pioneered in the Haplo setting, resulted in favorable rates of both acute and chronic GVHD¹
- Ease manageability and availability, low cost, no PTLD are other potential advantages of PTCy
- Use of PTCy has subsequently been expanded to other donor settings, i.e. HLA-identical sibling, MUD and MMUD, confirming its safety and efficacy as GVHD prophylactic agent^{2,3,4}

¹Luznik L et al. *Biol Blood Marrow Transplant* 2008

²Battipaglia G et al. *Cancer* 2021

³Ruggeri A et al. *J Hematol Oncol* 2018

⁴Battipaglia G et al. *Blood* 2019

ATG vs PTCy: pick up the winner

ATG



PTCy

ATG vs PTCy in UD allo-HSCT

Reference	Population	Donor type	N	Grade II-IV aGVHD	Grade III-IV aGVHD	All grades cGVHD	RI	NRM	PFS	OS	GRFS
Nykolyszyn 2020 (Marseille)	Hem malignancies PBSC	1-Ag MMUD	ATG, n=40 PTCy, n=22	35% 14%	18% 0%	26% 29%	32% 15%	22% 5%	45% 81%	56% 85%	27% 60%
Modi 2021 (USA)	AML, MDS	1-Ag MMUD	ATG, n=51 PTCy, n=25	52.9% 24.4%	19.6% 12%	49% 16%	15.7% 17%	31.4% 17%	52.9% 66%	56.9% 70.3%	21.6% 55.5%
Moiseev 2016 (Russian federation)	AML, ALL PBSC	MUD 1 or 2-Ag MMUD	ATG, n=125 PTCy, n=86	45% 19%	27% 4%	65% 16%	27% 19%	36% 16%	38% 65%	40% 69%	12% 52%
Ballen 2020 (Spain)	Hem malignancies	MUD 1-Ag MMUD	ATG, n=60 PTCy, n=72	67% 46%	34% 3%	23% 24%	22% 26%	24% 22%	51% 50%	58% 60%	44% 40%
Battipaglia, 2019 (EBMT)	AML	1-Ag MMUD	ATG, n=179 PTCy, n=93	32% 30%	19% 9%	36% 39%	37% 29%	29% 16%	34% 55%	38% 56%	21% 37%
Brissot, 2020 (EBMT)	AML	MUD	ATG, n=1452 PTCy, n=154	29.2% 28.8%	9% 8.8%	33.6% 31.4%	23.7% 25.2%	16.7% 15.2%	59.6% 59.7%	64.8% 62.7%	49.3% 41.6%



ATG vs PTCy: pick up the winner

ATG



PTCy

10/10 MUD allo-HSCT

ATG vs PTCy in 10/10 MUD: GVHD

Table 2 Cumulative incidence of GVHD

	180-day acute GVHD II-IV	180-day acute GVHD III-IV	2-year chronic GVHD	2-year ext. chronic GVHD
PTCY	28.8% [22.2–35.7]	8.8% [5.1–13.7]	31.4% [23.3–39.8]	18.5% [12–26.1]
ATG	29.2% [26.8–31.6]	9% [7.6–10.6]	33.6% [31–36.2]	13.1% [11.2–15]
p value	0.68	0.89	0.43	0.11

Abbreviations: *ATG* antithymocyte globulin, *Ext* extensive, *GVHD* graft-versus host disease, *PTCY* post-transplantation cyclophosphamide

No differences in GVHD incidence

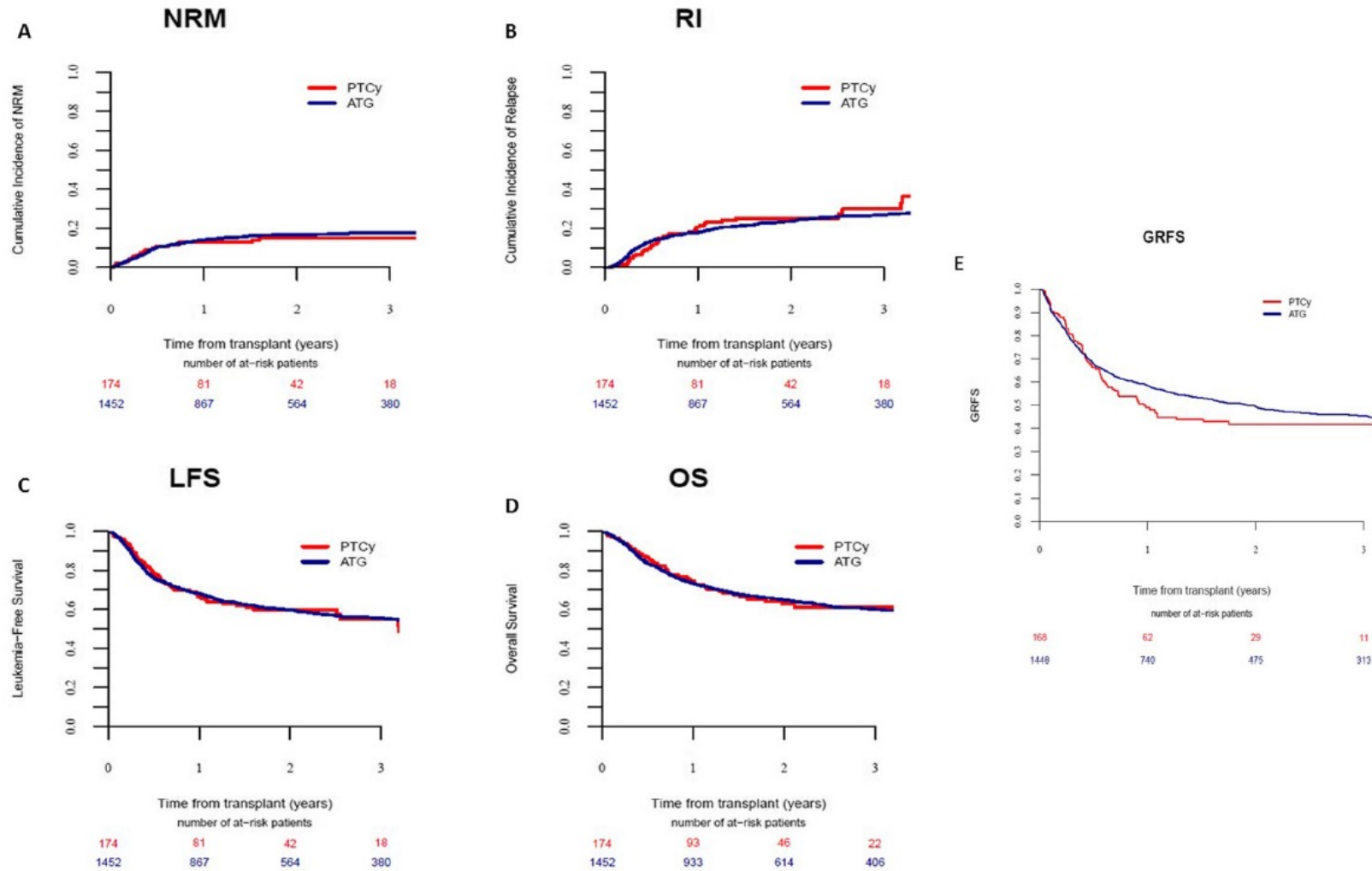
Table 3 Multivariate analysis for GVHD

	Acute GVHD II-IV		Acute GVHD III-IV		Chronic GVHD		Ext. chronic GVHD	
	HR (95% CI)	p value	HR (95% CI)	p value	HR (95% CI)	p value	HR (95% CI)	p value
ATG vs PTCY	0.98 (0.66–1.46)	0.93	0.84 (0.42–1.71)	0.64	1.22 (0.79–1.87)	0.37	0.64 (0.37–1.09)	0.09
Age (per 10 years)	1 (0.91–1.09)	0.92	1.01 (0.86–1.18)	0.92	1.06 (0.97–1.16)	0.20	1.03 (0.89–1.18)	0.73
sec. AML vs de novo	1.23 (0.95–1.61)	0.12	1.26 (0.79–2)	0.34	1.01 (0.76–1.33)	0.96	1.62 (1.1–2.39)	0.01
Adverse cytogenetics vs other	0.94 (0.74–1.21)	0.65	1.12 (0.73–1.71)	0.60	0.73 (0.56–0.96)	0.03	0.61 (0.39–0.95)	0.03
Female donor-male recipient vs other	1.27 (0.96–1.68)	0.10	1.67 (1.05–2.66)	0.03	1.07 (0.79–1.45)	0.65	1.05 (0.66–1.67)	0.83
RIC vs MAC	0.79 (0.62–1)	0.046	0.89 (0.59–1.36)	0.60	0.97 (0.76–1.23)	0.79	0.78 (0.54–1.14)	0.20
KPS ≥ 90	0.83 (0.65–1.06)	0.13	0.64 (0.42–0.97)	0.03	0.91 (0.71–1.17)	0.45	0.92 (0.63–1.34)	0.67
Patient CMV positivity	1.05 (0.85–1.31)	0.64	1.01 (0.68–1.48)	0.98	1.28 (1.03–1.6)	0.03	1.05 (0.75–1.47)	0.77
Donor CMV positivity	1 (0.81–1.23)	0.99	1.06 (0.73–1.53)	0.77	0.97 (0.79–1.2)	0.80	1.32 (0.96–1.82)	0.09
Year of transplantation	1.01 (0.96–1.06)	0.75	1.03 (0.94–1.12)	0.57	1 (0.95–1.05)	0.94	1.07 (0.99–1.16)	0.09
PBSC vs BM	1.05 (0.75–1.47)	0.77	1.1 (0.6–2)	0.76	1.1 (0.78–1.55)	0.59	1.37 (0.79–2.4)	0.26

Brissot E et al. *J Hematol Oncol* 2020



ATG vs PTCy in 10/10 MUD: survival



No differences in survival outcomes

Brissot E et al. J Hematol Oncol 2020



ATG vs PTCy in 10/10 MUD: available data

- no differences between the two GVHD prophylaxis strategies
- PTCy is safe and feasible in 10/10 MUD allo-HSCT

ATG vs PTCy: pick up the winner

ATG



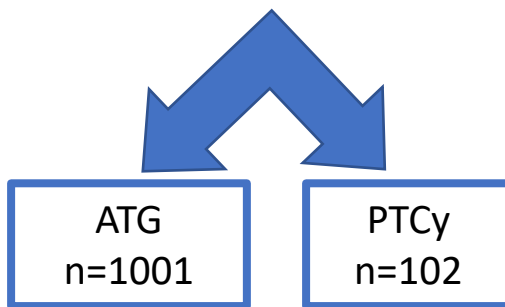
PTCy

What about 1-Ag MMUD allo-HSCT?

Posttransplant cyclophosphamide vs antithymocyte globulin in HLA-mismatched unrelated donor transplantation

Giorgia Battipaglia,^{1,2} Myriam Labopin,^{1,3,4} Nicolaus Kröger,⁵ Antonin Vitek,⁶ Boris Afanasyev,⁷ Inken Hilgendorf,⁸ Johannes Schetelig,⁹ Arnold Ganser,¹⁰ Didier Blaise,¹¹ Maija Itälä-Remes,¹² Jakob R. Passweg,¹³ Francesca Bonifazi,¹⁴ Jurgen Finke,¹⁵ Annalisa Ruggeri,¹⁶ Arnon Nagler,^{3,17} and Mohamad Mohty^{1,3,4}

Inclusion criteria
Age ≥ 18 years
Diagnosis of AML (all disease status allowed)
Transplant from 1Ag-MMUD
High-resolution HLA-allele typing available in EBMT registry
Use of either ATG or PTCy as GVHD prevention strategy
Transplant performed between 2011-2017

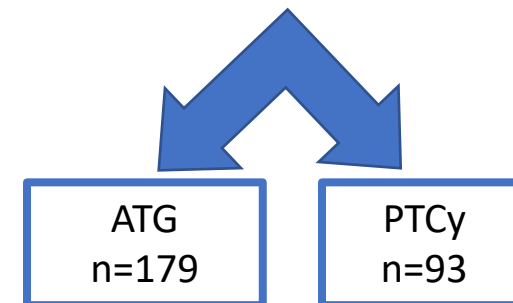


Propensity score matching was performed to reduce and eliminate confounding effects:

Each identified PTCy was matched with 2 ATG using the nearest neighbor or exact matching

Factors included in the propensity score model were:

Disease status at time of allo-HSCT, conditioning regimen, age, secondary AML, female donor to male recipient, source of stem cells, patient and donor CMV serology status.



Patients and transplant characteristics (after pair-matching)

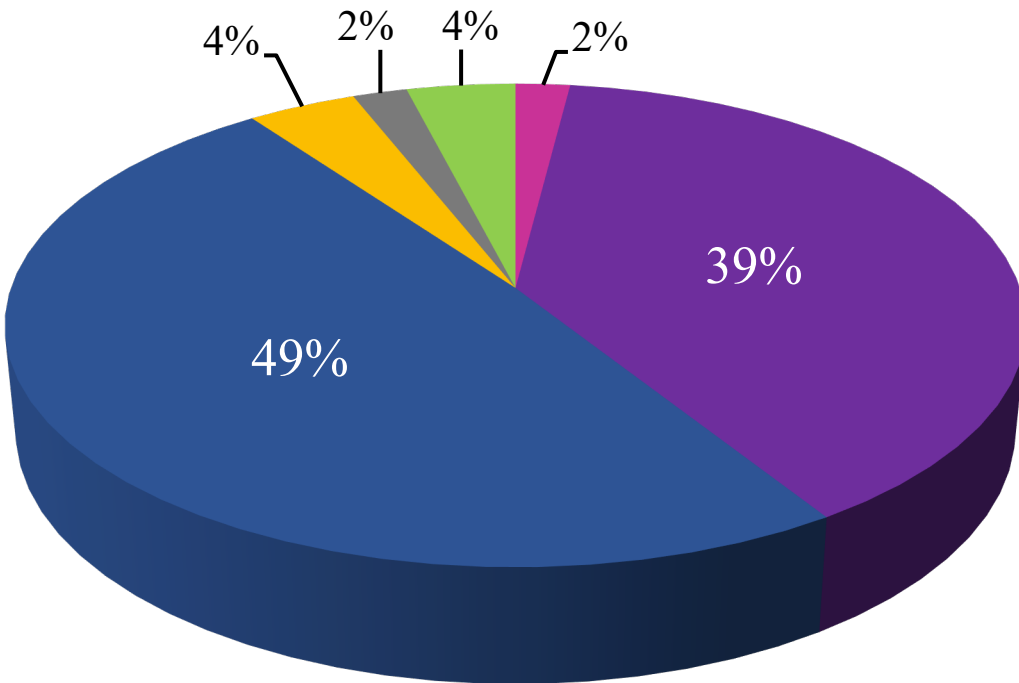
Characteristics	ATG, n=179 (%)	PTCy, n=93 (%)	p-value
Median age at allo-HSCT, years (range)	53 (19-75)	51 (20-73)	0.98
F/M	81 (45) / 98(55)	56(60) / 37(40)	<0.02
Secondary AML	36 (20)	17 (18)	0.72
Disease status at allo-HSCT			0.99
CR1	100 (56)	51 (55)	
CR2/3	28 (16)	15 (16)	
Active disease	51 (28)	27 (29)	
Karnofsky performance status < 80%	12 (7)	3 (3)	0.24
Female donor into male recipient	18 (10)	10 (11)	0.86
Interval from diagnosis to allo-HSCT, months (range)	6 (2-63)	6 (2-47)	0.98
Year of allo-HSCT (range)	2014 (2011-2017)	2015 (2011-2017)	<0.01
Conditioning regimen			0.97
MAC	90 (50)	47 (50)	
RIC	89 (50)	46 (50)	
Source of stem cells			0.95
BM	15 (8)	8 (9)	
PBSC	164 (92)	85 (91)	
Median follow-up, months (range)	27 (2-83)	14 (2-56)	<0.01

Battipaglia G et al. Blood 2019

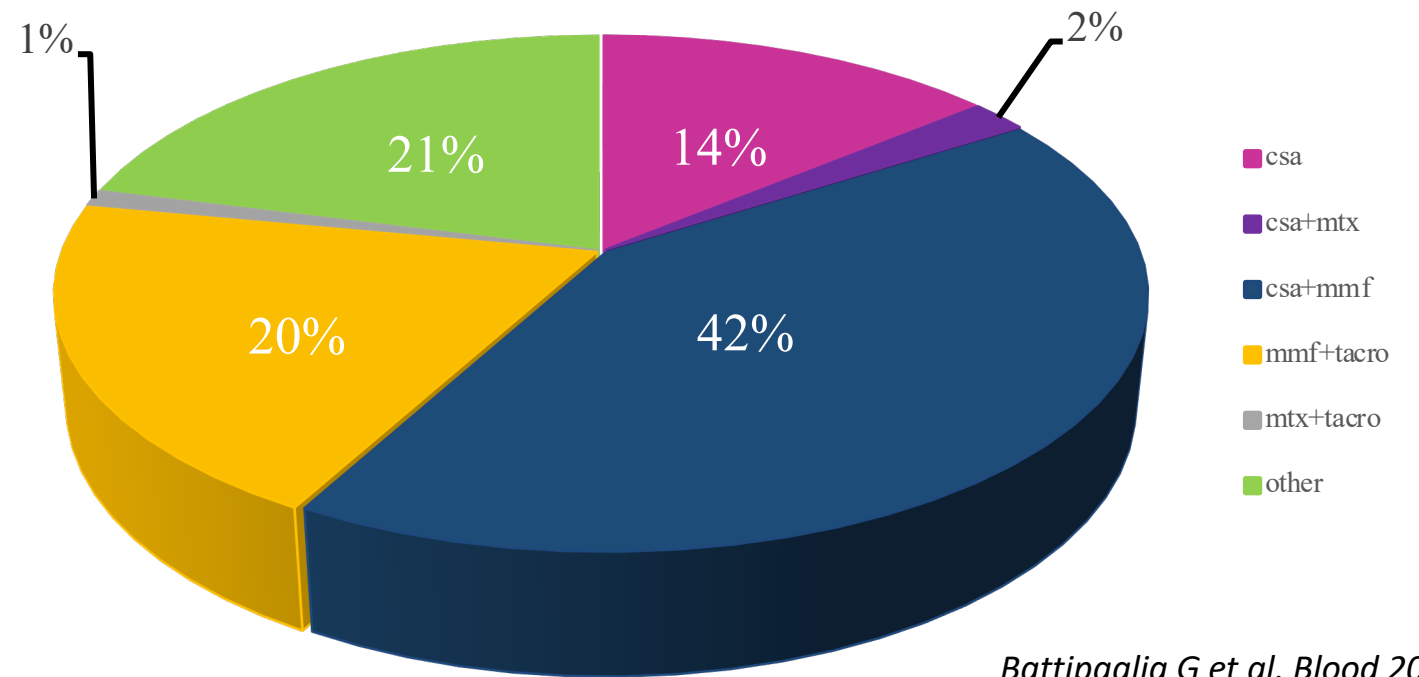


Associated GVHD prophylaxis

ATG (n=179)



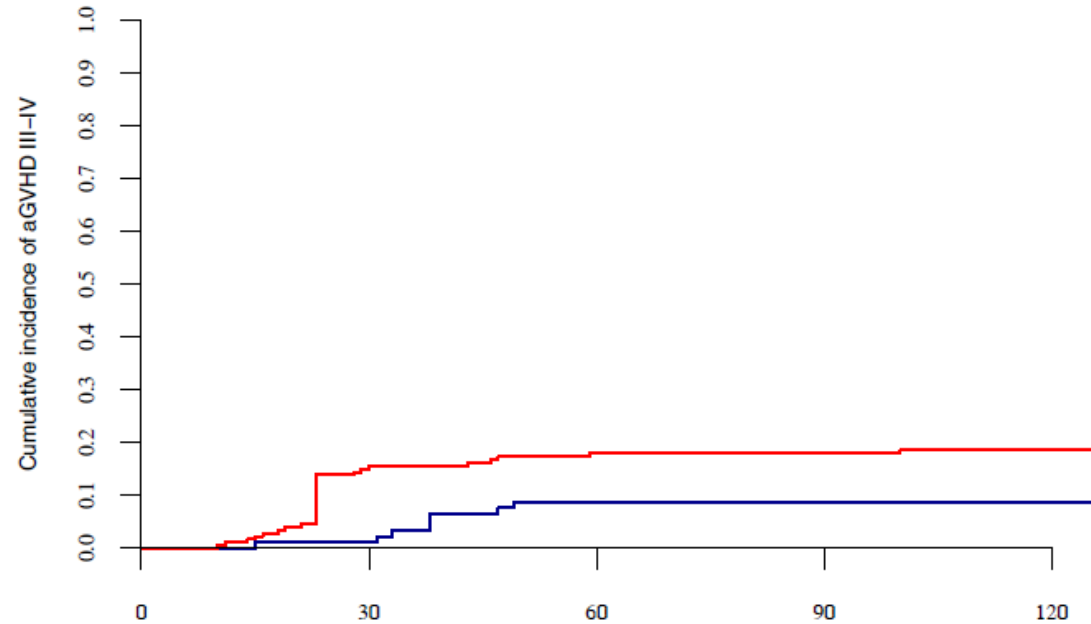
PTCy (n=93)



Battipaglia G et al. Blood 2019

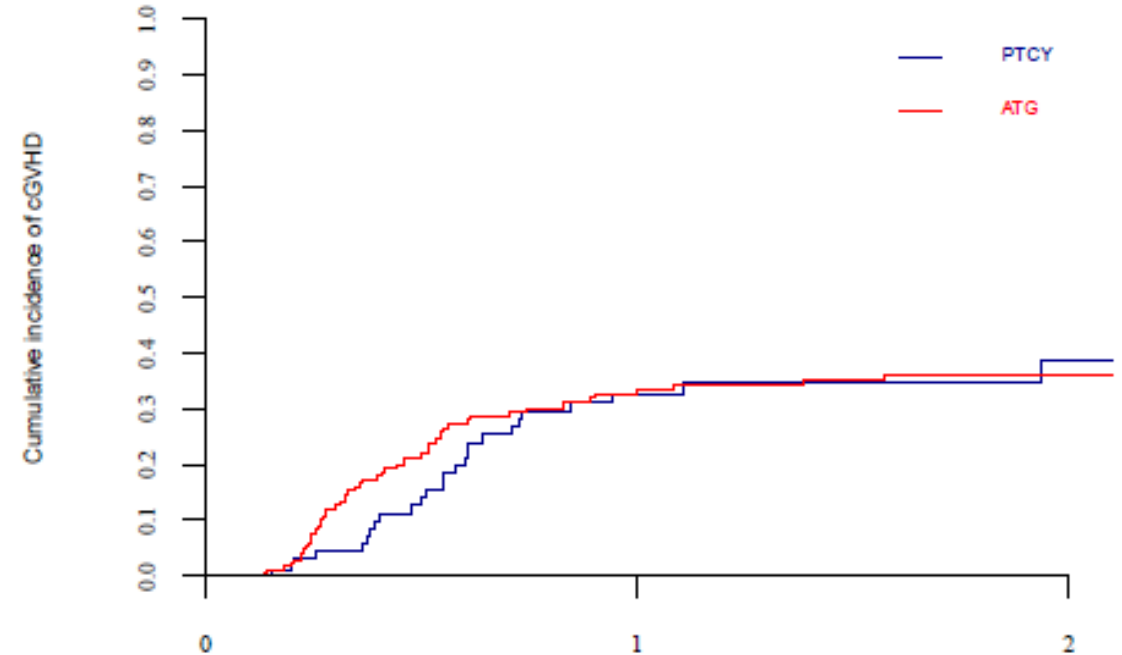
Acute and chronic GVHD

Grade III-IV aGVHD@100d



	Grade II-IV aGVHD, % [95% CI]	Grade III-IV aGVHD, % [95% CI]
PTCy	30 [21-40]	9 [4-16]
ATG	32 [26-40]	19 [13-25]
P-value	0.39	0.03

cGVHD@2y

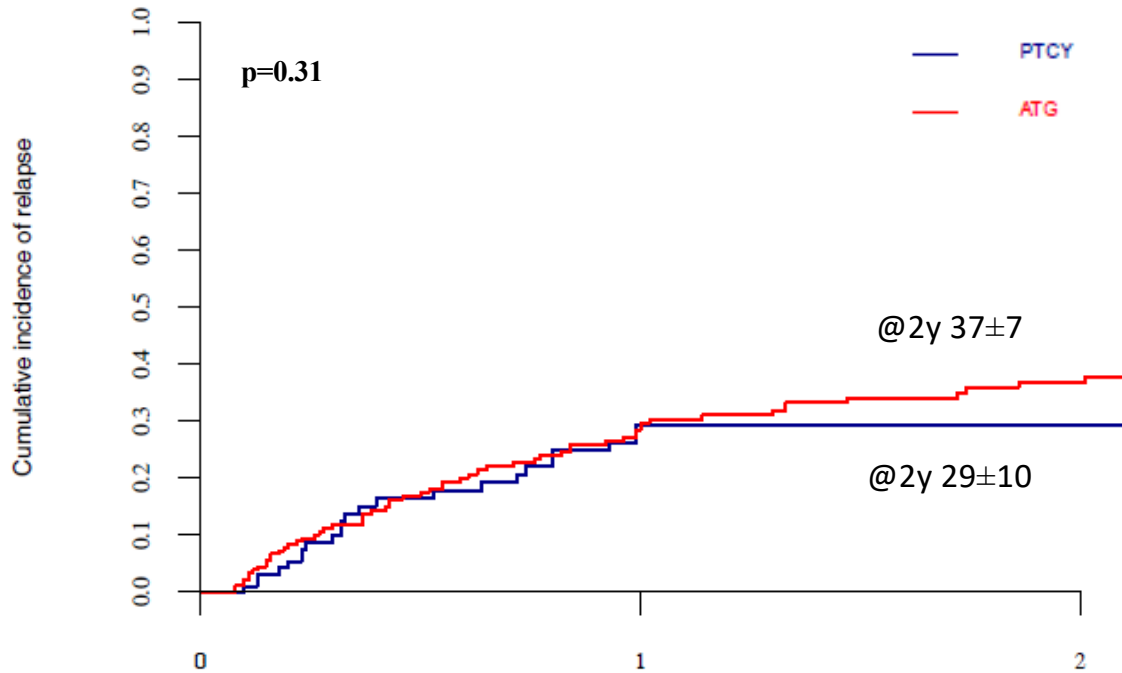


	cGVHD, % [95% CI]	Extensive cGVHD, % [95% CI]
PTCy	39 [26-51]	17 [8-28]
ATG	36 [28-44]	20 [14-28]
P-value	0.35	0.31

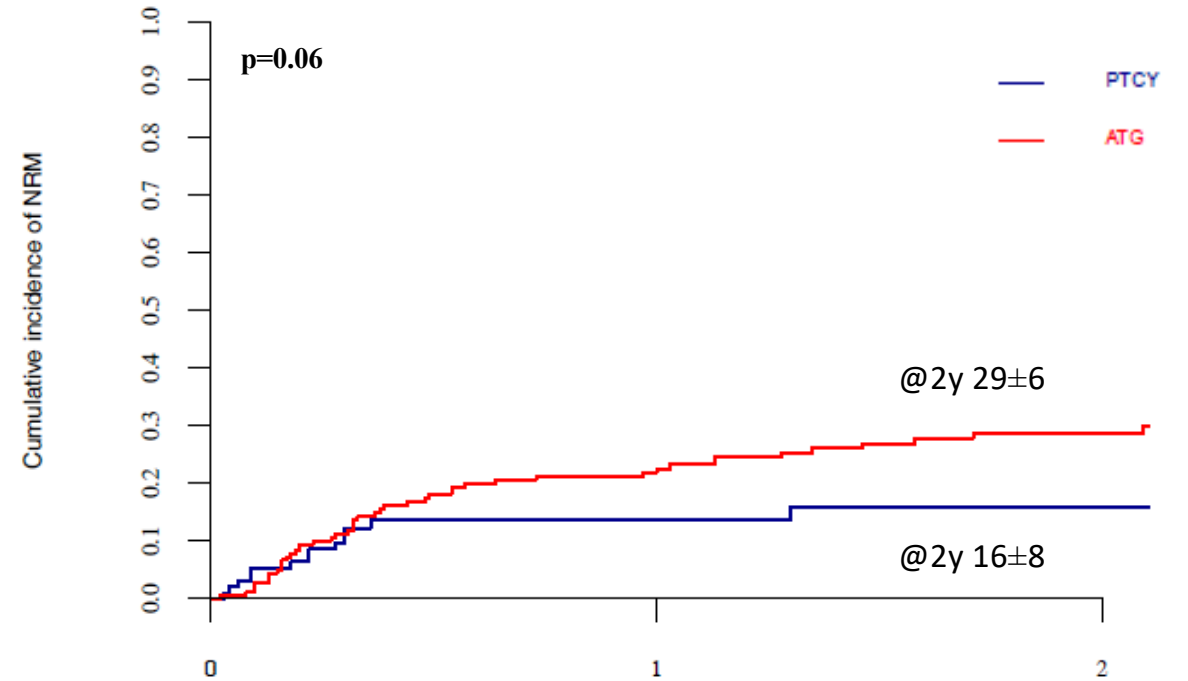
Battipaglia G et al. Blood 2019

RI and NRM at 2 years

RI



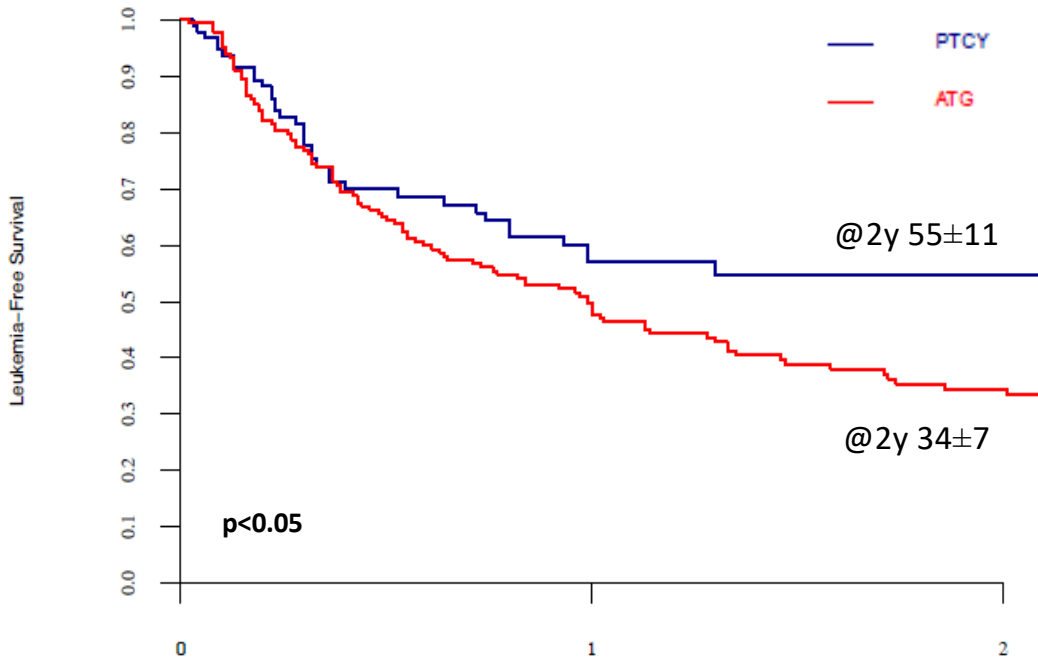
NRM



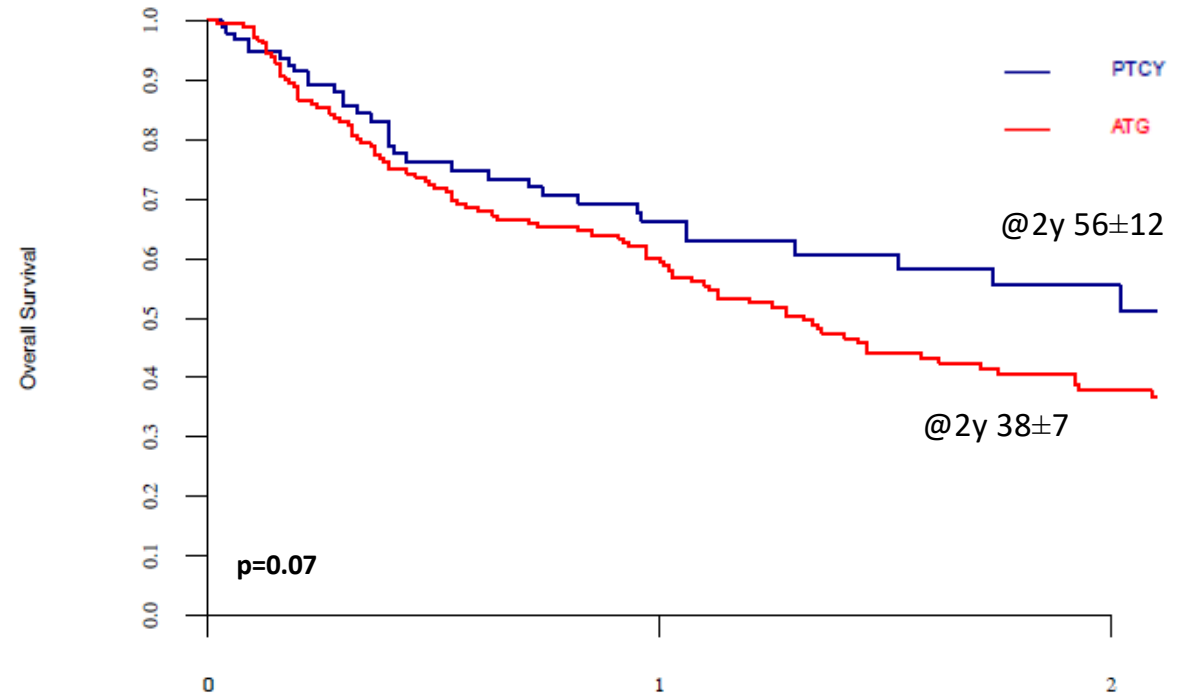
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LFS and OS at 2 years

LFS

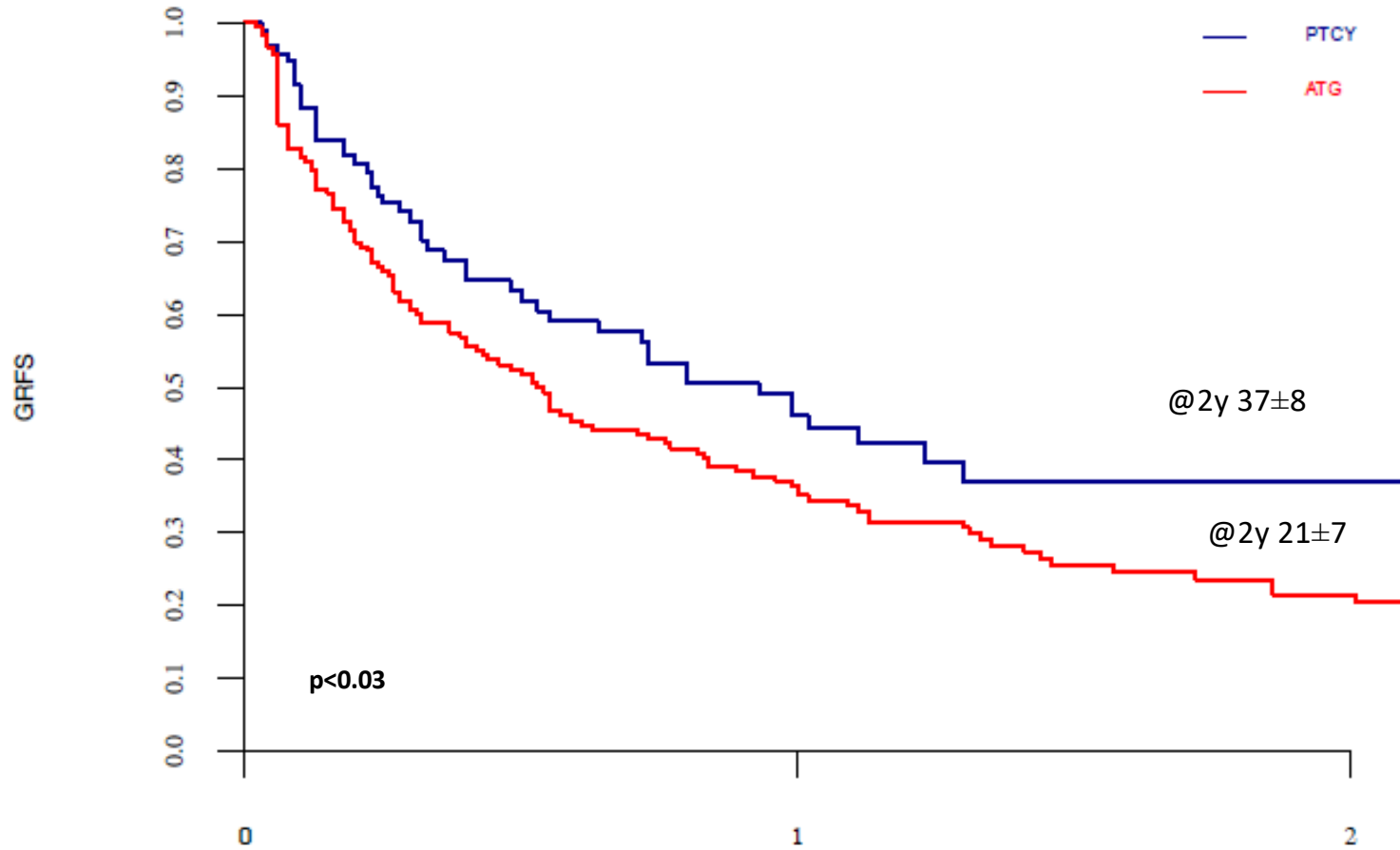


OS



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GRFS at 2 years



Battipaglia G et al. Blood 2019

Subgroups analysis: PTCY or ATG with CsA+MMF

	Grade II-IV aGVHD, % [95% CI]	Grade III-IV aGVHD, % [95% CI]	2y-cGVHD, any grade [95% CI]	2y-cGVHD, extensive [95% CI]
PTCy (n=38)	27 [14-42]	8 [2-19]	28 [13-46]	19 [5-40]
ATG (n=87)	36 [26-47]	22 [14-32]	31 [21-42]	21 [12-31]
P-value	0.23	0.07	0.42	0.48

	LFS, % [95% CI]	OS, % [95% CI]	GRFS [95% CI]	RI [95% CI]	NRM [95% CI]
PTCy (n=38)	58 [41-76]	59 [41-77]	40 [19-60]	31 [15-48]	11 [3-23]
ATG (n=87)	29 [19-39]	33 [22-43]	14 [6-22]	38 [27-49]	33 [22-43]
P-value	0.08	0.12	<0.02	0.52	0.07

Battipaglia G et al. Blood 2019



Subgroups analysis: CR at allo-HSCT

	Grade II-IV aGVHD, % [95% CI]	Grade III-IV aGVHD, % [95% CI]	2y-cGVHD, any grade [95% CI]	2y-cGVHD, extensive [95% CI]
PTCY (n=66)	32 [21-43]	8 [3-16]	45 [28-60]	21 [10-34]
ATG (n=128)	30 [22-38]	16 [10-24]	37 [28-46]	23 [15-32]
P-value	0.98	0.10	0.71	0.74

	LFS, % [95% CI]	OS, % [95% CI]	GRFS [95% CI]	RI [95% CI]	NRM [95% CI]
PTCY (n=66)	63 [50-77]	63 [48-78]	41 [26-56]	22 [12-34]	14 [6-26]
ATG (n=128)	42 [33-52]	45 [35-54]	25 [16-34]	30 [22-39]	27 [19-36]
P-value	0.04	<0.05	<0.05	0.29	0.13

Battipaglia G et al. Blood 2019



Subgroups analysis: PBSC as stem cell source

	Grade II-IV aGVHD, % [95% CI]	Grade III-IV aGVHD, % [95% CI]	2y-cGVHD, any grade [95% CI]	2y-cGVHD, extensive [95% CI]
PTCY (n=85)	29 [20-39]	8 [4-16]	38 [24-51]	19 [10-31]
ATG (n=164)	32 [25-39]	18 [13-25]	36 [28-44]	20 [14-28]
P-value	0.41	0.04	0.61	0.72

	LFS, % [95% CI]	OS, % [95% CI]	GRFS [95% CI]	RI [95% CI]	NRM [95% CI]
PTCY (n=85)	57 [45-69]	60 [48-72]	37 [24-50]	29 [19-40]	14 [7-24]
ATG (n=164)	34 [26-43]	38 [30-47]	23 [15-30]	37 [29-45]	28 [21-36]
P-value	0.03	0.04	0.03	0.48	0.04

Battipaglia G et al. Blood 2019



ATG vs PTCy in UD: metanalysis

In the setting of unrelated donor allo-HSCT, prophylaxis based on PTCy compared to ATG has shown to be associated to:

- Lower incidence of grade II-IV aGVHD
- Lower incidence of grade III-IV aGVHD
- Lower NRM and EBV-related complications
- Higher OS

No differences between the 2 GVHD prophylaxis strategies in terms of:

- cGVHD
- RI
- CMV reactivation and BKV-related HC

Tang L et al. Front Oncol 2023

Is PTCy the answer?

- Studies comparing Haplo to UD showed no differences in transplant outcomes^{1,2}

PTCy-
MMUD
















PTCy-Haplo

¹Piemontese S J Hematol Oncol 2017

²Ciurea et al, Blood 2015

Post-transplant cyclophosphamide in one-antigen mismatched unrelated donor transplantation versus haploidentical transplantation in acute myeloid leukemia: a study from the Acute Leukemia Working Party of the EBMT

Giorgia Battipaglia ^{1,2}✉, Jacques-Emmanuel Galimard ³, Myriam Labopin ^{3,4,5}, Anna Maria Raiola⁶, Didier Blaise ⁷, Annalisa Ruggeri ⁸, Yener Koc⁹, Zafer Gülbas¹⁰, Antonin Vitek¹¹, Simona Sica¹², Jose Luiz Diez-Martin¹³, Luca Castagna¹⁴, Benedetto Bruno¹⁵, Montserrat Rovira¹⁶, Ivan Moiseev ¹⁷, Massimo Martino ¹⁸, Giovanni Grillo¹⁹, Mercedes Colorado Araujo²⁰, Claude Eric Bulabois²¹, Stéphanie Nguyen²², Gerard Socié ²³, Mutlu Arat ²⁴, Jiri Pavlu²⁵, Johanna Tischer²⁶, Hans Martin²⁷, Lucia Lopez Corral²⁸, Goda Choi²⁹, Edouard Forcade ³⁰, Andrew McDonald³¹, Fabrizio Pane^{1,2}, Ali Bazarbachi ³², Fabio Ciceri ⁸, Amon Nagler ^{3,33} and Mohamad Mohty^{3,4,5}

Inclusion criteria

Age ≥ 18 years

Diagnosis of AML in CR1 or CR2

First allo-HCT from Haplo or MMUD

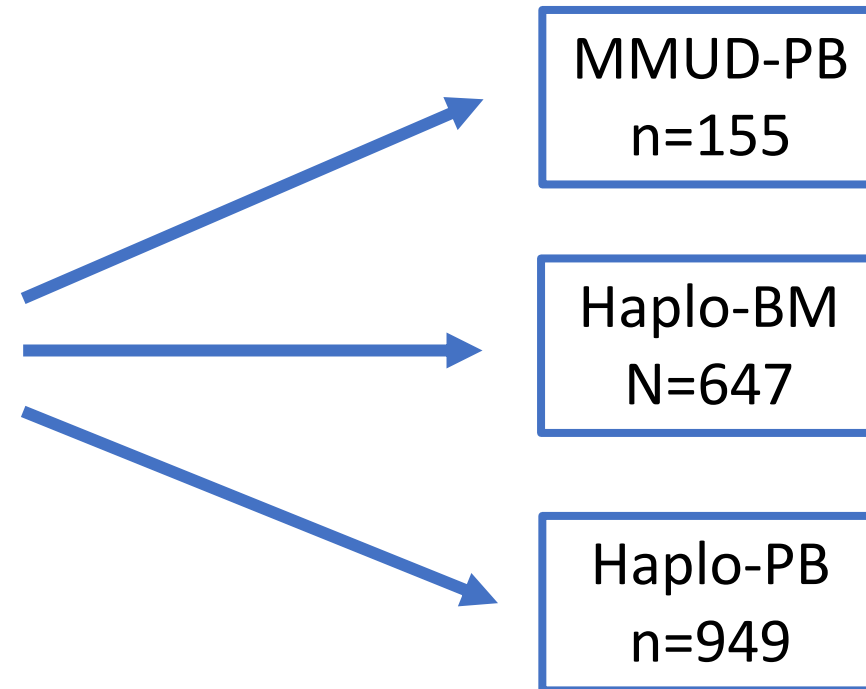
Use of PTCy as GVHD prophylaxis

Transplant performed between 2009-2019

Exclusion criteria

In vivo T-cell depletion with ATG or alemtuzumab

Ex vivo T-cell depletion



Patients and transplant characteristics

Characteristics (%)	MMUD-PB, n=155	Haplo-BM, n=647	Haplo-PB, n=949	p-value
Median age at allo-HSCT, years (range)	52 (18-79)	52 (18-79)	55 (18-76)	<0.01
Age > 55	70 (45)	298 (46)	510 (54)	
F/M	67 (43) / 88 (57)	287 (44) / 359 (56)	413 (43.5) / 536 (56.5)	0.93
Secondary AML	31 (20)	65 (10)	148 (16)	<0.01
Disease status at allo-HCT				0.22
CR1	124 (80)	474 (73)	712 (75)	
CR2	31 (20)	173 (27)	237 (25)	
HLA mismatch				
Class I	119 (77)	-	-	
Class II	36 (23)	-	-	
Karnofsky performance status < 90	35 (24)	125 (20)	214 (24)	0.24
Female donor to male recipient	17 (11)	131 (20)	196 (21)	0.02
Interval from diagnosis to allo-HSCT, months (range)	5.7 (1.3-86.3)	6.2 (1.8-82.6)	5.9 (0.8-154.9)	0.16
Year of allo-HSCT (range)	2018 (2012-2019)	2016 (2009-2019)	2017 (2010-2019)	<0.01
Conditioning regimen				<0.01
RIC	72 (46.5)	190 (29.4)	394 (41.5)	
MAC	83 (53.5)	457 (70.6)	555 (58.5)	
Median follow-up, years (95% CI)	1.9 (1.3 - 2.1)	3 (2.7 - 3.3)	1.9 (1.7 - 2)	-

Battipaglia G et al. Bone Marrow Transplant 2022



Results

- The most frequently used conditioning regimen in the Haplo- setting was TBF, both as MAC and RIC. Flu-Cy-TBI was also frequently used as RIC.
- Bu-Flu followed by TBF were the preferred conditioning regimens, both as MAC and RIC, in the MMUD-PB group. Flu-Cy-TBI was also frequently used as RIC.
- A CNI (mainly CsA) with MMF were the most frequent adjuvant immunosuppressive agents in all groups.
- At 30 days, CI of neutrophil engraftment was 92%, 88% and 90% in MMUD-PB, Haplo-BM and Haplo-PB, respectively ($p=0.01$)
- Median time to neutrophil engraftment was 15 (range 5-42), 19 (range 1-62) and 16 (range 1-78) in MMUD-PB, Haplo-BM and Haplo-PB, respectively.

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Results: acute and chronic GVHD

Univariate analysis

Outcome [95% CI]	MMUD-PB	Haplo-BM	Haplo-PB	p-value
Grade II-IV aGVHD@100 days	30 [23-38]	20 [17-23]	32 [29-35]	<0.01
Grade III-IV aGVHD@100 days	12 [7-18]	5 [4-8]	12 [10-14]	<0.01
cGVHD all grades@2 years*	34 [25-43]	26 [22-29]	34 [30-37]	0.01
Extensive cGVHD@2 years*	14 [8-22]	9 [7-11]	13 [10-15]	0.09

*Due to the longer follow-up in Haplo-BM, outcomes were censored at 2 years.

Multivariate analysis*

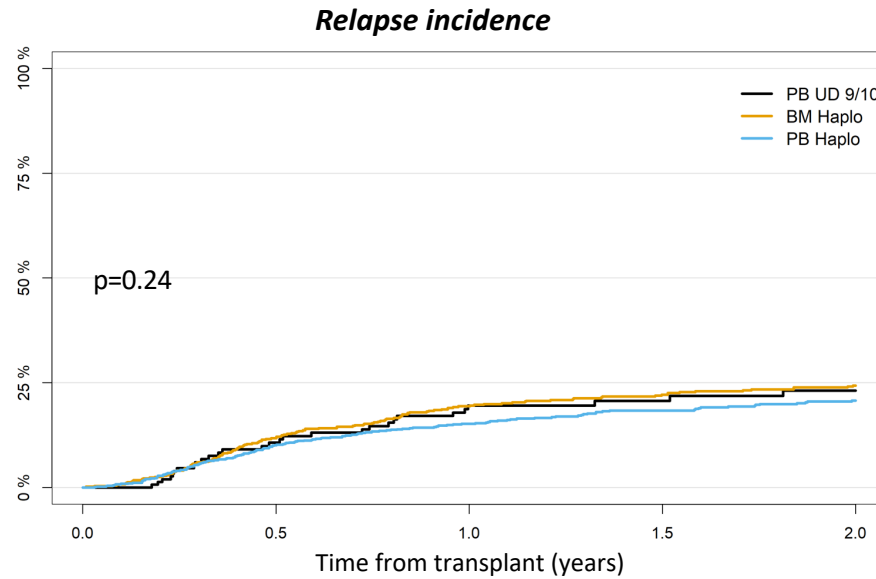
	Grade II-IV Acute GVHD		Grade III-IV Acute GVHD		Chronic GVHD, all grades		Chronic GVHD, extensive	
	HR (95% CI)	p value	HR (95% CI)	p value	HR (95% CI)	p value	HR (95% CI)	p value
MMUD-PB (ref)	1		1		1		1	
Haplo-BM	0.70 (0.47-1.03)	0.07	0.44 (0.24-0.81)	<0.01	0.74 (0.42-1.29)	0.29	0.87 (0.35-2.14)	0.76
Haplo-PB	1.17 (0.83-1.65)	0.37	1.05 (0.63-1.78)	0.84	1.08 (0.66-1.78)	0.76	1.17 (0.51-2.66)	0.71

*Adjusted for donor type and stem cell source, secondary AML, F donor to M recipient, conditioning regimen intensity, age, year of transplant, patient CMV serology, disease status at transplant (CR1 vs CR2)

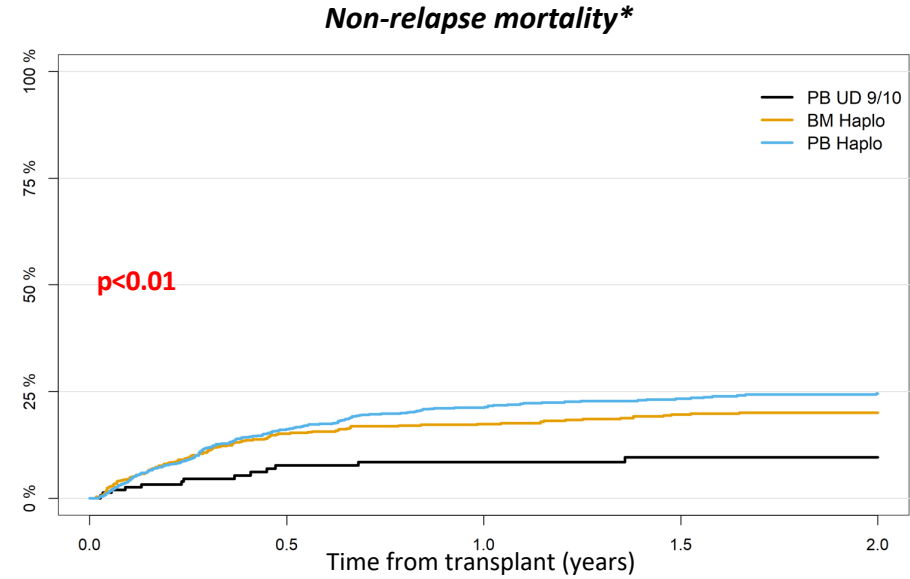
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Results: NRM and RI

Due to the longer follow-up in Haplo-BM, outcomes were censored at 2 years.



	RI [95% CI]
MMUD-PB	23 [16-31]
Haplo-BM	24 [21-28]
Haplo-PB	21 [18-24]



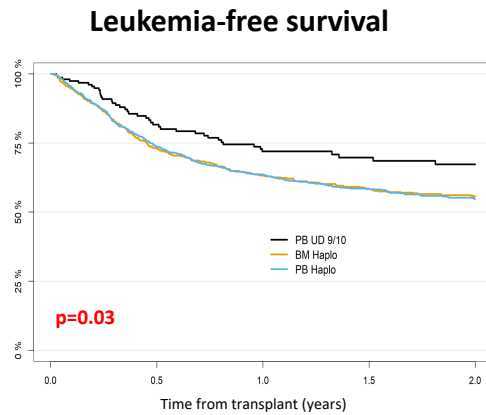
	NRM [95% CI]
MMUD-PB	10 [5-15]
Haplo-BM	20 [17-23]
Haplo-PB	24 [21-27]

*main cause of death was attributable to infections in the Haplo groups (Haplo-BM 28%, Haplo-PB 27% versus 11% in MMUD-PB)

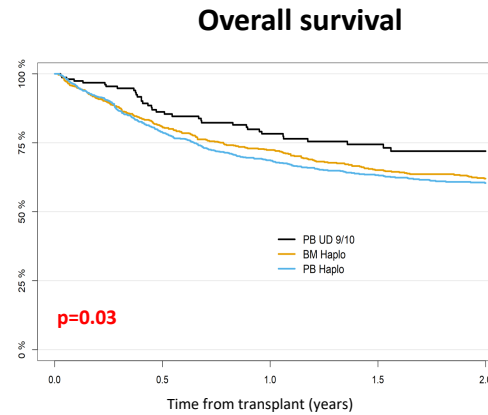
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Results: LFS, OS and GRFS

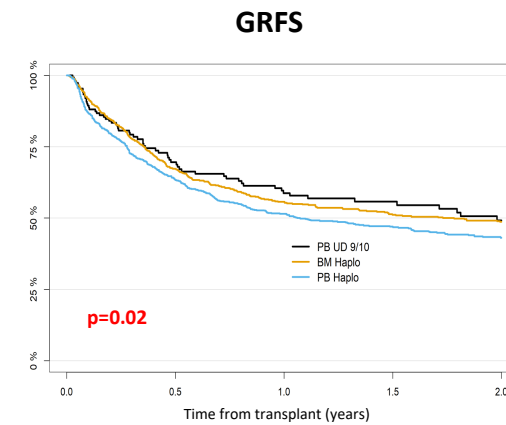
Due to the longer follow-up in Haplo-BM, outcomes were censored at 2 years.



	LFS [95% CI]
MMUD-PB	67 [58-75]
Haplo-BM	56 [51-60]
Haplo-PB	55 [51-58]



	OS [95% CI]
MMUD-PB	72 [63-79]
Haplo-BM	62 [58-66]
Haplo-PB	60 [57-64]



	GRFS [95% CI]
MMUD-PB	49 [39-58]
Haplo-BM	49 [44-53]
Haplo-PB	43 [39-47]

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Results: MV analysis for survival

Multivariate analysis for RI and NRM*

	RI		NRM	
	HR (95% CI)	p value	HR (95% CI)	p value
MMUD-PB (ref)	1		1	
Haplo-BM	1.21 (0.80-1.83)	0.36	2.28 (1.23-4.24)	<0.01
Haplo-PB	0.96 (0.64-1.43)	0.83	2.65 (1.46-4.81)	<0.01

Multivariate analysis for LFS, OS and GRFS

	LFS		OS		GRFS	
	HR (95% CI)	p value	HR (95% CI)	p value		
MMUD-PB (ref)	1		1		1	
Haplo-BM	1.51 (1.06-2.14)	0.02	1.50 (1.02-2.21)	0.04	1.02 (0.76-1.36)	0.91
Haplo-PB	1.47 (1.05-2.05)	0.02	1.51 (1.05-2.19)	0.03	1.19 (0.91-1.56)	0.20

*Adjusted for donor type and stem cell source, secondary AML, F donor to M recipient, conditioning regimen intensity, age, year of transplant, patient CMV serology, disease status at transplant (CR1 vs CR2)

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Conclusions

- Available data are still not mature to promote the use of PTCy over ATG in the 10/10 MUD
- Despite mainly retrospective, available data in the 1-Ag MMUD setting favor the use of PTCy over ATG as GVHD prophylaxis
- When facing the “alternative donor” options, preferring a 1-Ag MMUD with PTCy over a Haplo (if timing allows) should be considered



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GRAZIE PER L'ATTENZIONE

