The role of Anti-thymocyte globulin with Thiotepa-Busulfan-fludarabine based conditioning in patients undergoing haploidentical stem cell transplant and post-transplant cyclophosphamide.

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Background

- The Thiotepa-Busulfan-Fludarabine (TBF) based conditioning regimen is widely used in T replete haploidentical transplantation (Haplo) with post-transplant cyclophosphamide.
- However, the use of Anti-thymocyte globulin (ATG) has not been well established. It decreases the incidence of graft versus host disease (GvHD) however some claim that it’s at the cost of increased relapse.

Methods

- Multicentric retrospective study.
- Data was collected from:
  - American University of Beirut Medical Center,
  - Hopital Saint Antoine Paris,
  - Institute Paoli Calmette Marseille,
  - Humanitas Research Hospital Milan.
- We included all adult patients and who underwent haplo with TBF conditioning.
  - Thiotepa 5 mg/kg per day infused on days -7 and/or -6,
  - Fludarabine 30 mg/m2 infused on day -5 to day -2;
  - Busulfan 130 mg/m2 infused on day -5 to day -3.
  - Graft versus host disease (GVHD) prophylaxis:
    - cyclophosphamide 50 mg/kg per day on day +3 and day +5 or +4 ,
    - cyclosporine initiated at 1.5 mg/kg on day +6 and readjusted according to level
    - mycophenolate mofetil 500 mg every 6 hours beginning on days +6 to +28 or +35.
    - Patients who received ATG received a dose of 2.5 mg/kg per day on day -2 and day -1.

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Patients and transplant characteristics

Patients characteristics	No ATG N (%)	ATG N (%)	Total N (%)
Number of patients	199 (74)	69 (26)	268 (100)
Age at transplant median (range)	58 (16-72)	53 (14-72)	56 (14-72)
Female	77 (39)	24 (35)	101 (38)
Male	122 (61)	45 (65)	167 (62)
Disease type			
Lymphoma	22 (11)	5 (7)	27 (10)
Acute leukemia	126 (63)	42 (61)	168 (63)
Other	51 (26)	22 (32)	73 (27)

Transplant characteristics	No ATG N (%)	ATG N (%)	Total N (%)
Sorror ≤ 3	76 (40)	24 (75)	100 (37)
Sorror >3	112 (60)	8 (25)	120 (45)
Disease Risk Index			
low	25 (13)	25 (36)	50 (19)
intermediate	120 (60)	31 (45)	151 (56)
high	54 (27)	13 (19)	67 (25)
Disease Status at Transplant			
CR	141 (71)	48 (70)	189 (71)
PR	11 (5)	9 (13)	20 (7)
PD	47 (24)	12 (17)	59 (22)
Stem cell source			
PBSC	165 (83)	61 (88)	226 (84)
BM	34 (17)	8 (12)	42 (16)
stem cells Infused			
Infused CD34 x10 /kg	5.22 (1.4-18.1)	6.2 (1-10.4)	5.5 (1-18.1)
Infused CD3 x10 /kg	2.31 (1.33-70.6)	3.48 (1.34-34)	2.11 (1.33-70.6)
Thiotepa days			
1 day	59 (30)	50 (73)	109 (41)
2 days	140 (70)	19 (27)	159 (59)
Days of ATG			
One day ATG	0 (0)	31 (45)	31 (12)
Two days ATG	0 (0)	38 (55)	38 (14)

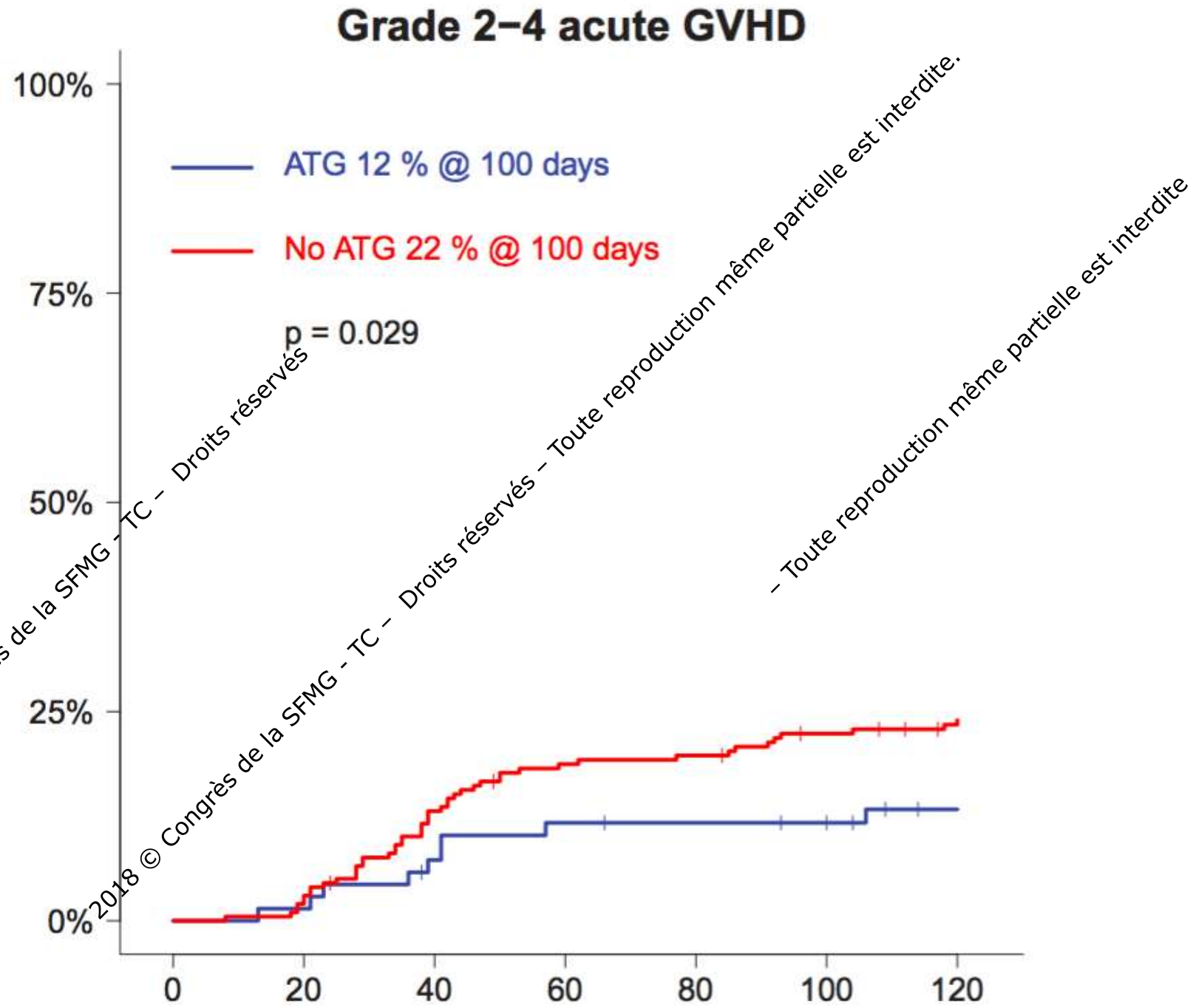
Univariate analysis

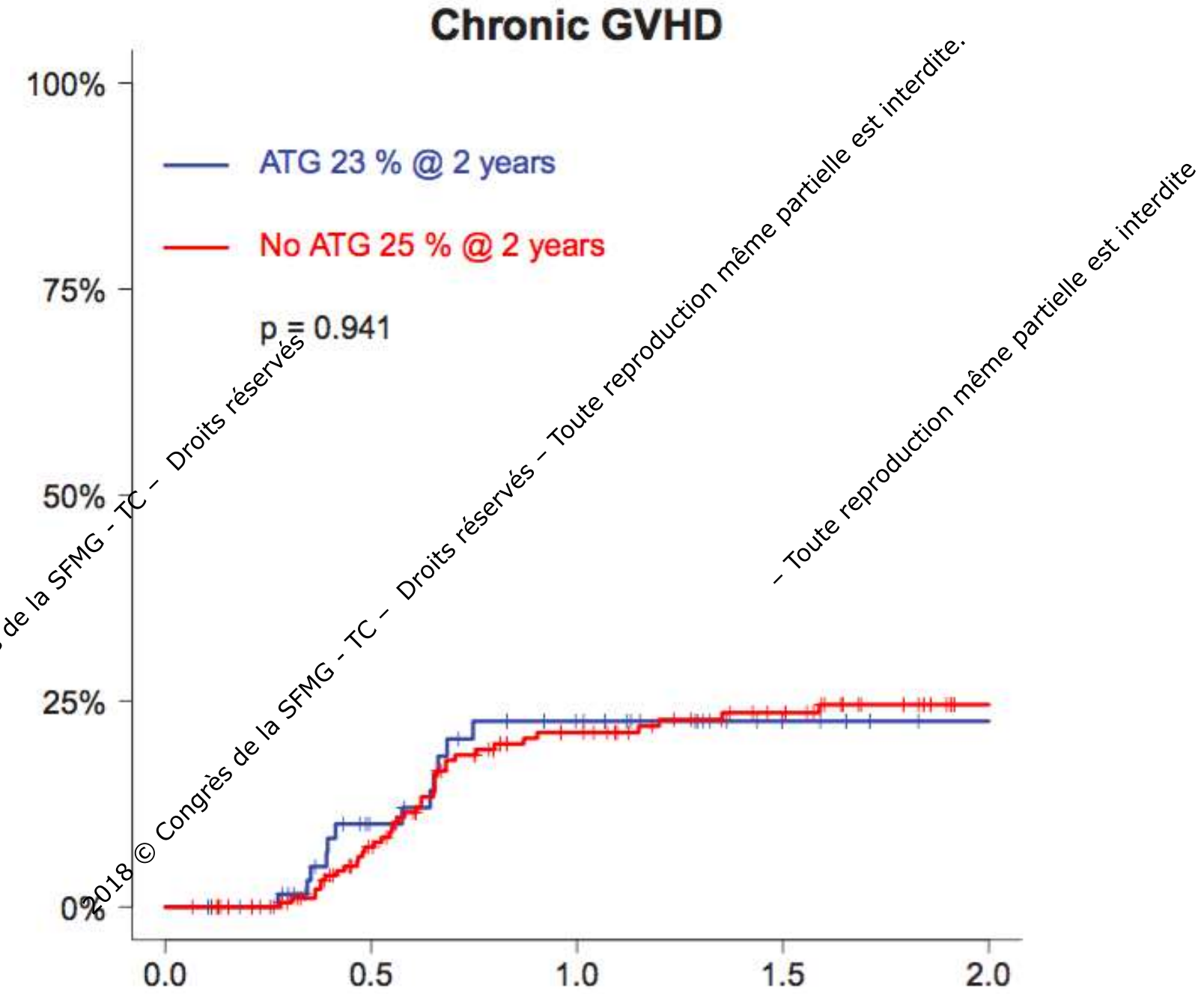
	ATG N (%)	No ATG N (%)	Total N (%)	P
aGVHD gr II-IV	8 (12)	44 (22)	54 (20)	**0.029**
12 months				
cGVHD	16 (23)	42 (21)	59 (22)	0.929
NRM	6 (8)	46 (23)	51 (19)	**0.005**
CIR	17 (25)	34 (17)	51 (19)	0.221
PFS	46 (67)	119 (60)	166 (62)	0.179
OS	55 (79)	137 (69)	190 (71)	**0.029**
GRFS	31 (45)	92 (46)	123 (46)	0.831
at 24 months				
CGVH all grades	16 (23)	50 (25)	64 (24)	0.929
NRM	6 (8)	52 (26	59 (22)	**0.005**
CIR	20 (29)	42 (21)	62 (23)	0.221
PFS	43 (63)	105 (53)	150 (56)	0.179
OS	55 (79)	123 (62)	177 (66)	**0.029**
GRFS	31 (45)	86 (43)	118 (44)	0.831

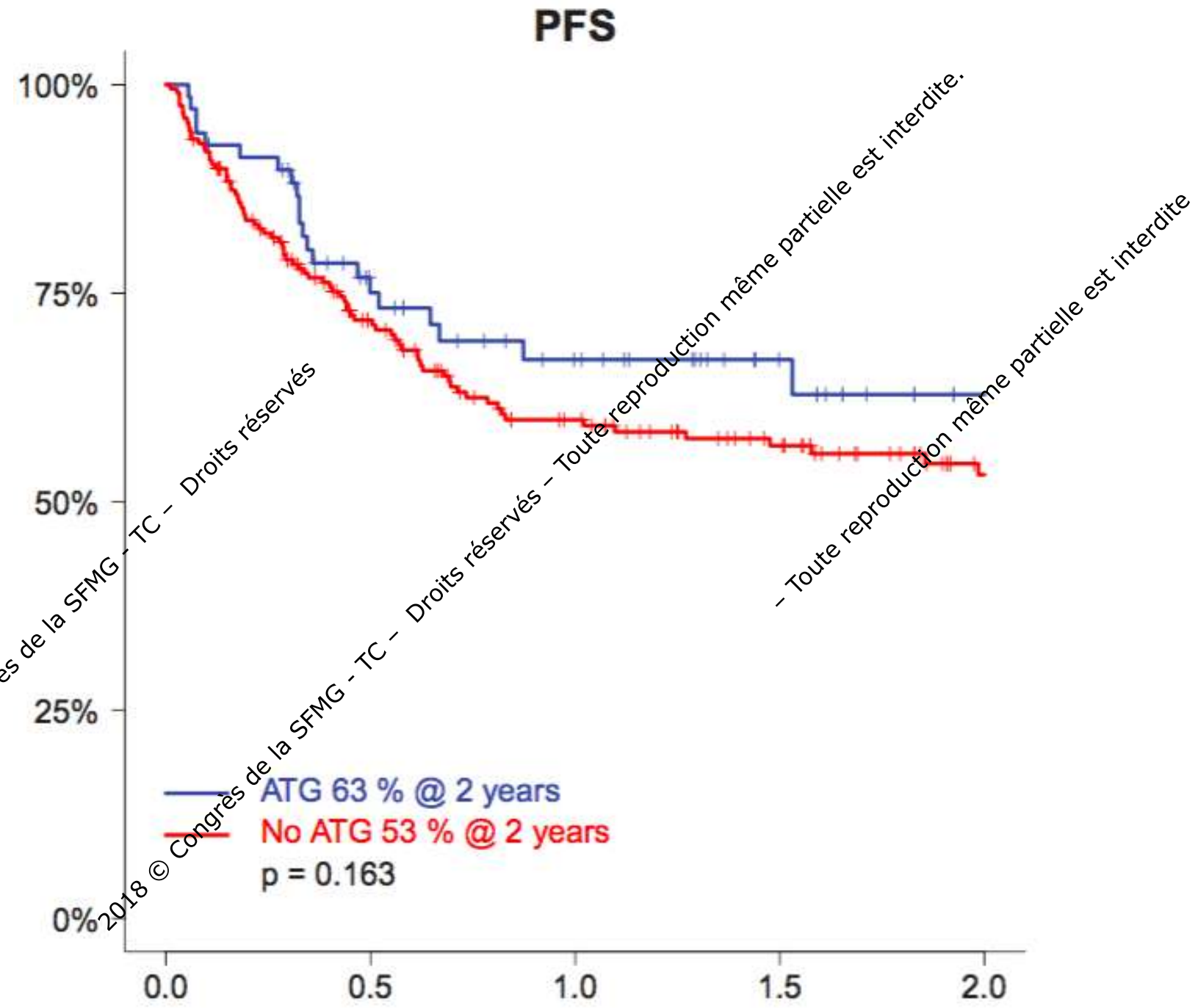
Multivariate analysis

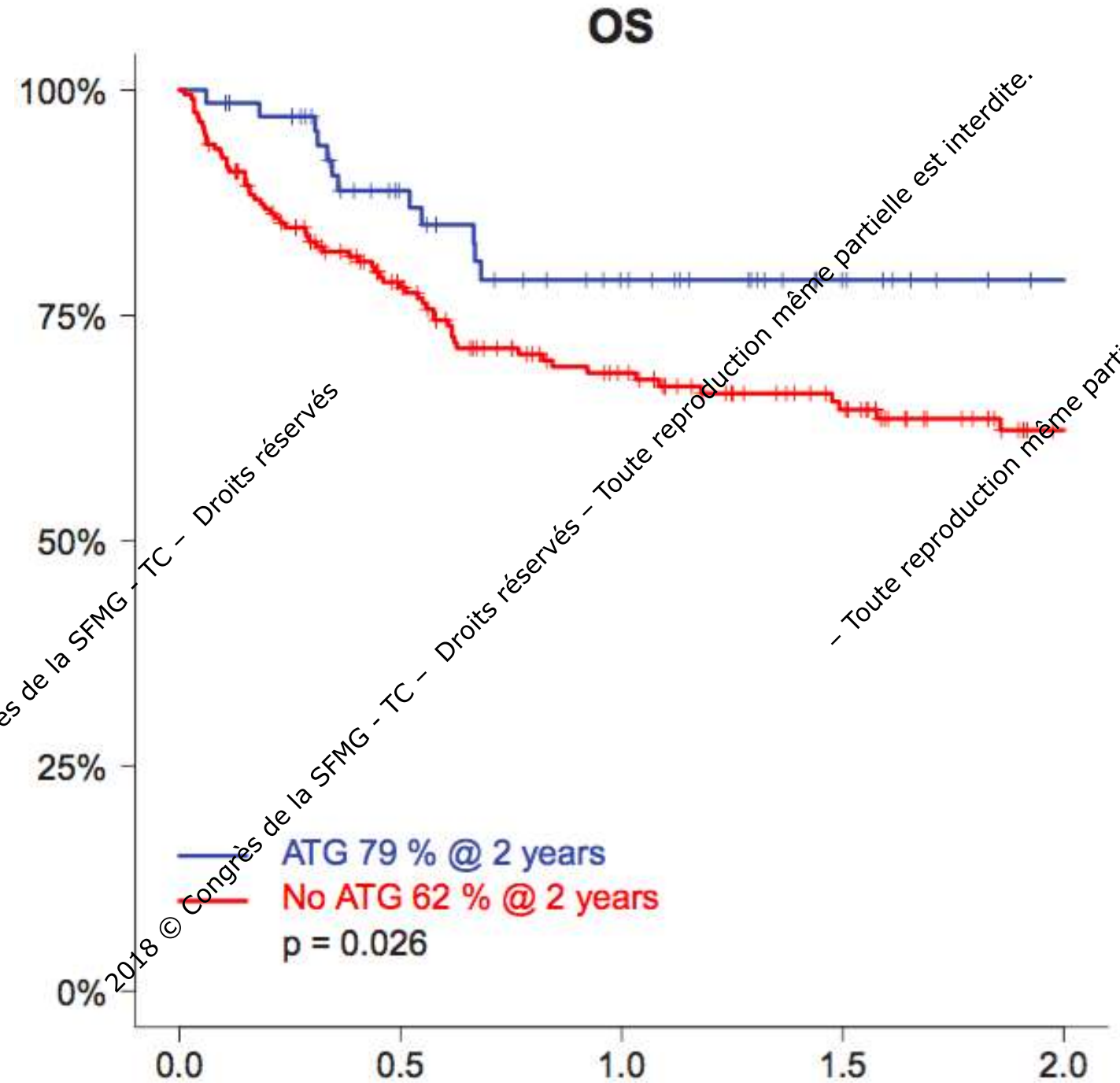
	aGVHD G-II-IV		cGVHD		NRM		CIR	
	HR CI95	p			HR CI95	p	HR CI95	
ATG vs no ATG	1.86 (0.66 - 5.21)	0.239	0.66 (0.21 - 2.05)	0.473	1.44 (0.40 - 5.23)	0.577	0.98 (0.40 - 2.41)	0.967
Age	0.99 (0.97 - 1.01)	0.512	0.99 (0.96 - 1.01)	0.372	1.01 (0.99 - 1.04)	0.437	**0.98 (0.96 - 1.00)**	**0.062**
DRI intermediate	1.13 (0.61 - 2.09)	0.708	0.85 (0.41 - 1.77)	0.673	0.77 (0.42 - 1.40)	0.385	0.70 (0.34 - 1.46)	0.346
DRI low	0.53 (0.17 - 1.66)	0.274	0.63 (0.18 - 2.23)	0.471	**0.28 (0.06 - 1.23)**	**0.092**	0.72 (0.25 - 2.08)	0.542
Sorror >=3	1.00 (0.58 - 1.73)	0.991	1.50 (0.76 - 2.95)	0.242	**2.32 (1.18 - 4.55)**	**0.014**	0.74 (0.39 - 1.40)	0.354
Thiotepa2 days	0.74 (0.40 - 1.37)	0.342	1.76 (0.76 - 4.05)	0.187	0.94 (0.48 - 1.83)	0.846	**0.52 (0.27 - 1.02)**	**0.059**
cd34	**1.08 (1.00 - 1.17)**	**0.058**	1.02 (0.93 - 1.12)	0.722	1.00 (0.91 - 1.10)	0.989	**1.12 (1.02 - 1.23)**	**0.017**
PBSC	1.62 (0.65 - 4.03)	0.297	0.98 (0.40 - 2.42)	0.971	2.06 (0.70 - 6.13)	0.191	0.82 (0.34 - 1.96)	0.65

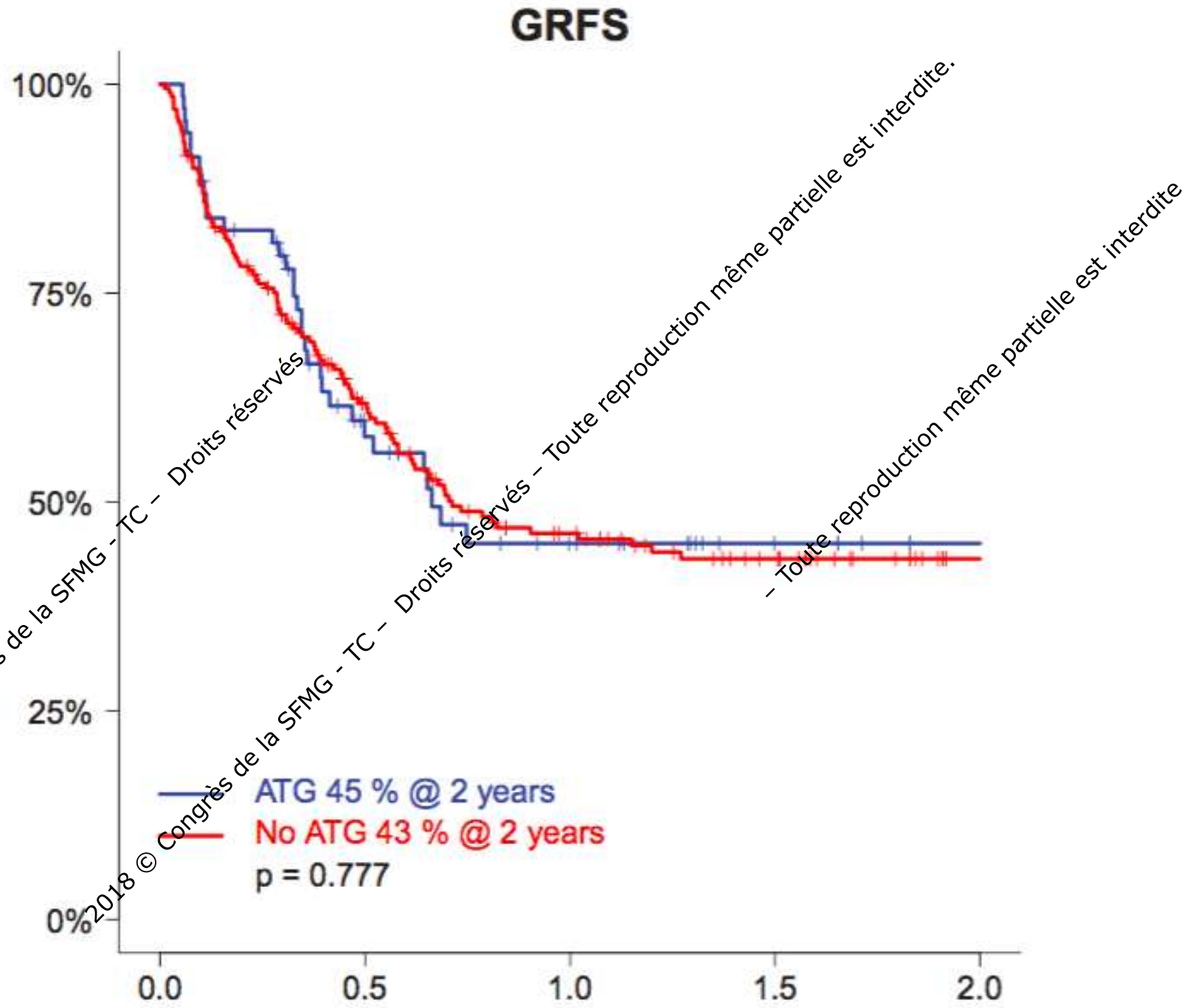
	PFS		OS		GRFS	
	HR CI95	p	HR CI95	p	HR CI95	p
ATG vs no ATG	1.10 (0.54 - 2.27)	0.78	1.00 (0.43 - 2.32)	0.993	0.77 (0.41 - 1.46)	0.427
Age	0.99 (0.98 - 1.01)	0.454	1.00 (0.98 - 1.02)	0.929	0.99 (0.98 - 1.01)	0.498
DRI intermediate	0.75 (0.47 - 1.19)	0.224	0.72 (0.44 - 1.19)	0.2	0.85 (0.56 - 1.29)	0.449
DRI low	0.52 (0.23 - 1.18)	0.117	**0.36 (0.13 - 0.98)**	**0.045**	**0.50 (0.24 - 1.03)**	**0.059**
Sorror >=3	1.28 (0.83 - 1.99)	0.263	**1.70 (1.03 - 2.82)**	**0.039**	1.26 (0.86 - 1.86)	0.241
Thiotepa2 days	0.72 (0.45 - 1.16)	0.18	0.71 (0.42 - 1.20)	0.204	0.84 (0.55 - 1.30)	0.435
cd34	**1.06 (0.99 - 1.13)**	**0.085**	1.01 (0.93 - 1.10)	0.802	1.05 (0.99 - 1.11)	0.141
PBSC	1.29 (0.66 - 2.50)	0.457	1.02 (0.51 - 2.04)	0.951	1.06 (0.61 - 1.84)	0.846

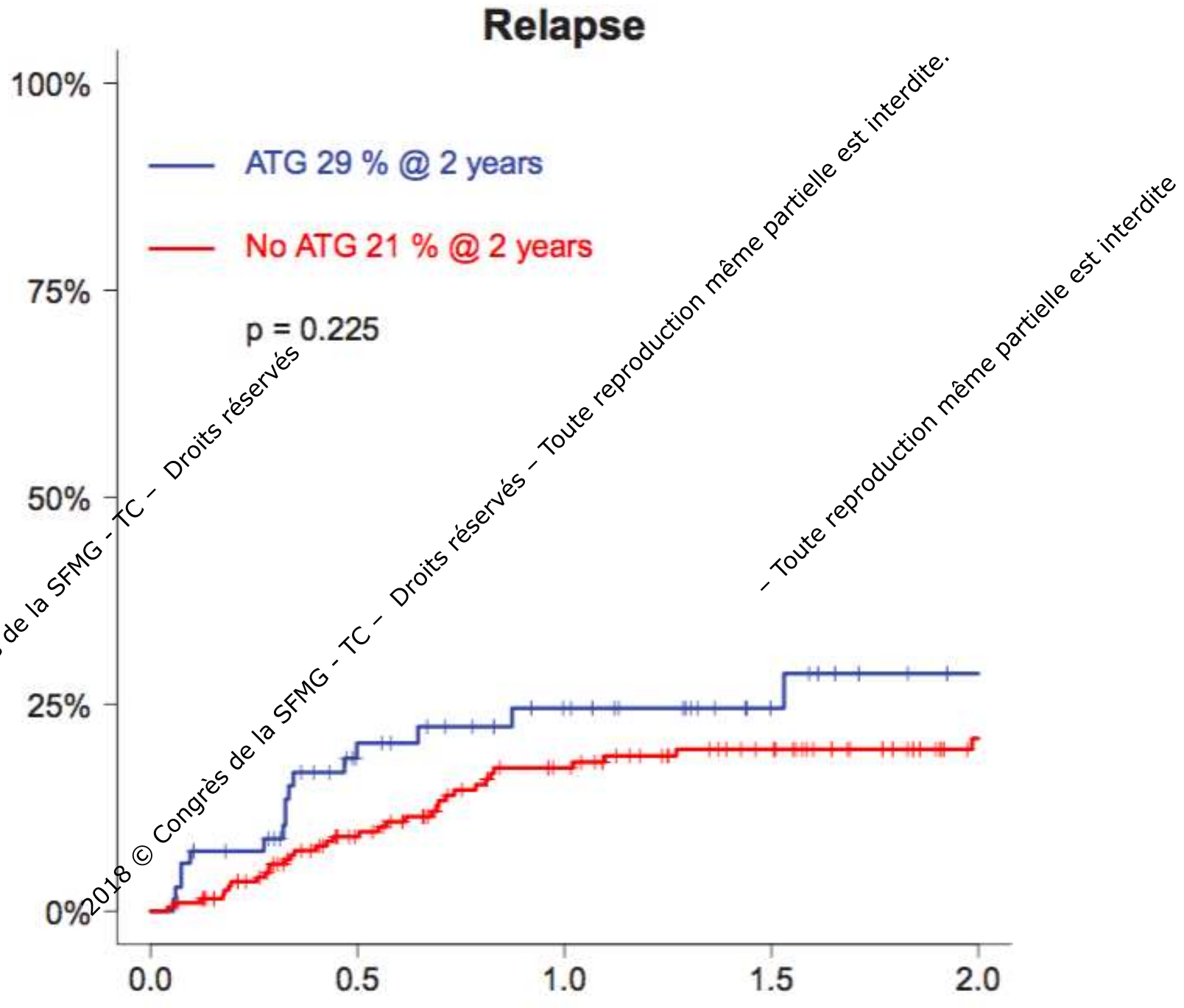


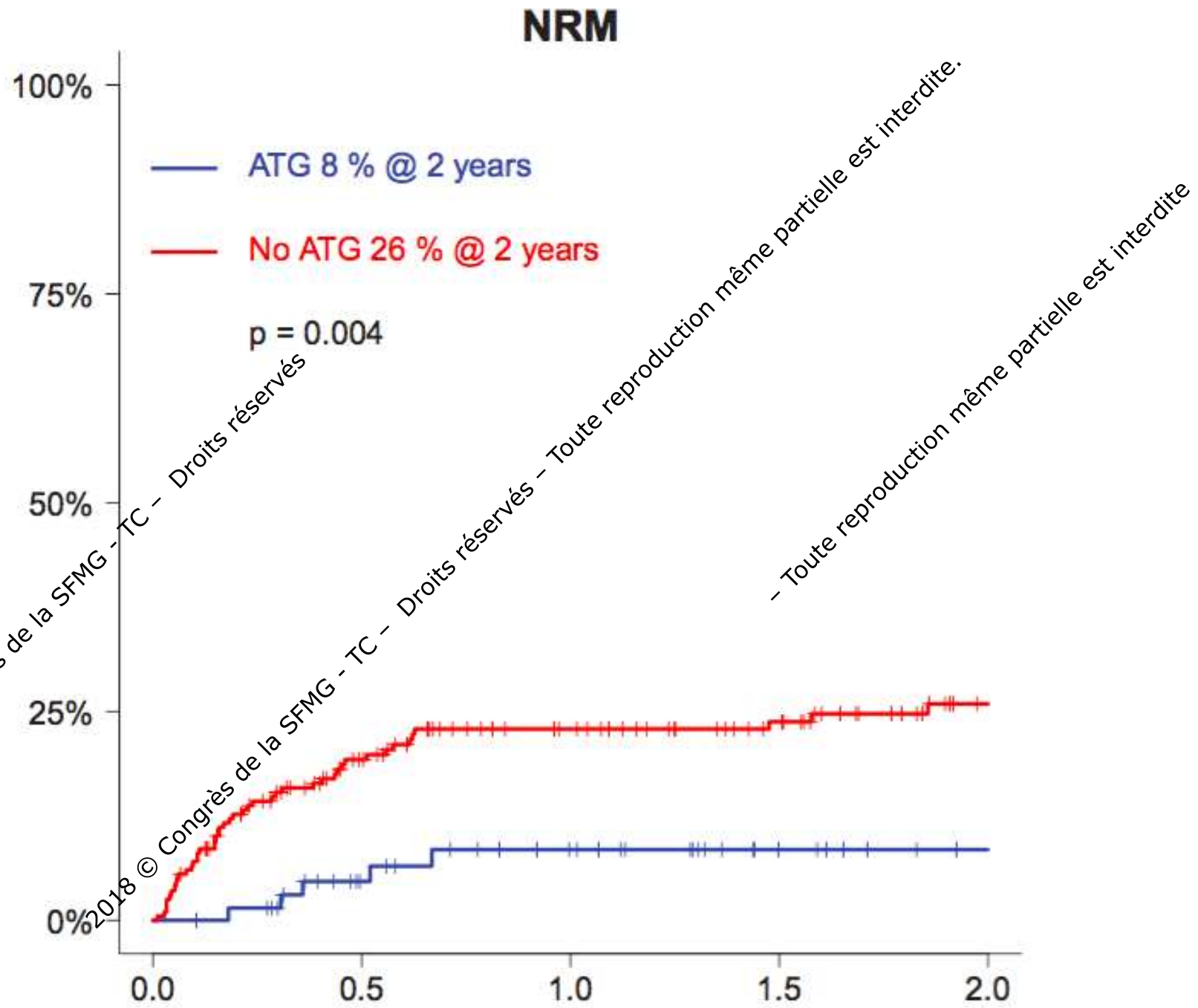












Conclusion

- ATG as part of the pre-transplantation conditioning leads to significant reduction in aGVHD and NRM at 24 months, and increases OS without significant effects on PFS.

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