Impact of ATG formulations on outcomes

As we did not have information of the brand of ATG, we performed following subgroup analysis by assuming that ATG at dose <16mg/Kg is Thymoglobin and dose 16 to 60 mg/Kg is Grafalon. These results should be interpreted with caution.

Supplementary table S1: Multivariate analysis of outcomes based on presumed ATG formulations based on dosages.

	RI		**NRM**		**LFS**		**OS**		**GRFS**	
	HR (95% CI)	p	HR (95% CI)	p	HR (95% CI)	p	HR (95% CI)	p	HR (95% CI)	p
No ATG (reference)										
Thymoglobin vs no	1.51 (0.82-2.78)	0.186	0.445 (0.222-0.892)	0.0224	0.853 (0.557-1.31)	0.466	0.785 (0.505-1.22)	0.281	0.789 (0.542-1.15)	0.214
Grafalon vs no	1.45 (0.847-2.47)	0.176	0.496 (0.252-0.974)	0.0417	0.899 (0.614-1.32)	0.587	0.868 (0.583-1.29)	0.485	0.78 (0.554-1.1)	0.155
age (per 10y)	1.09 (0.952-1.26)	0.206	1.21 (1-1.46)	0.048	1.12 (1.01-1.25)	0.0368	1.13 (1.01-1.27)	0.0348	1.08 (0.982-1.19)	0.111
Year of Tx	1.03 (0.96-1.1)	0.426	1.03 (0.942-1.12)	0.533	1.03 (0.981-1.09)	0.213	1.05 (0.991-1.11)	0.102	1.03 (0.983-1.08)	0.223
status at Tx										
CR2+ vs CR1	0.956 (0.597-1.53)	0.851	1.19 (0.703-2.03)	0.512	1.06 (0.754-1.49)	0.733	1.08 (0.758-1.54)	0.667	1 (0.748-1.34)	0.99
advanced vs CR1	2.36 (1.59-3.49)	1.91e-05	1.05 (0.536-2.05)	0.893	1.8 (1.3-2.5)	0.000415	1.73 (1.23-2.43)	0.00158	1.61 (1.2-2.17)	0.0017
cytogenetics										
interm. vs favorable	1.25 (0.734-2.14)	0.41	1.23 (0.676-2.24)	0.497	1.22 (0.825-1.79)	0.323	1.31 (0.872-1.97)	0.192	1.07 (0.781-1.46)	0.682
poor vs favorable	2.88 (1.67-4.96)	0.000138	1.42 (0.727-2.78)	0.305	2.21 (1.48-3.32)	0.00012	2.34 (1.53-3.59)	0,00009	1.57 (1.12-2.2)	0.00935
KPS>=90 % vs <90%	0.79 (0.543-1.15)	0.219	0.517 (0.329-0.813)	0.00424	0.695 (0.529-0.914)	0.00918	0.641 (0.484-0.849)	0.00193	0.802 (0.628-1.03)	0.0786
Donor type										
UD 10/10 vs MSD	0.708 (0.438-1.14)	0.159	2.87 (1.68-4.9)	0.000111	1.24 (0.887-1.73)	0.21	1.39 (0.983-1.96)	0.0622	1.13 (0.839-1.52)	0.424
UD 9/10 vs MSD	0.728 (0.388-1.37)	0.322	2.72 (1.36-5.45)	0.00463	1.23 (0.787-1.91)	0.368	1.34 (0.849-2.13)	0.207	1.46 (0.99-2.15)	0.0563

PB vs BM	1.64 (1.03-2.63)	0.0387	1.09 (0.641-1.85)	0.753	1.4 (1-1.95)	0.048	1.45 (1.02-2.05)	0.039	1.33 (1.01-1.77)	0.0443
F->M vs other	0.892 (0.603-1.32)	0.567	1.44 (0.903-2.29)	0.126	1.07 (0.801-1.44)	0.635	1.13 (0.832-1.53)	0.434	1.2 (0.939-1.54)	0.144
Pat. CMV pos vs neg	0.852 (0.617-1.18)	0.329	1.64 (1.06-2.55)	0.0274	1.04 (0.812-1.34)	0.741	1.1 (0.848-1.44)	0.463	1.07 (0.861-1.33)	0.546
Don. CMV pos vs neg.	0.735 (0.532-1.02)	0.0628	0.938 (0.617-1.43)	0.764	0.803 (0.625-1.03)	0.0864	0.868 (0.667-1.13)	0.29	0.858 (0.692-1.07)	0.165
FluTBI vs CyTBI	0.645 (0.344-1.21)	0.17	0.976 (0.461-2.07)	0.95	0.765 (0.488-1.2)	0.242	0.694 (0.427-1.13)	0.14	1.03 (0.715-1.5)	0.859
center (frailty)		0.211		0.181		0.9		0.902		0.255

	acute GVHD II-IV		**acute GVHD III-IV**		**chronic GVHD**		**ext. Chronic GVHD**	
	HR (95% CI)	p	HR (95% CI)	p	HR (95% CI)	p	HR (95% CI)	p
No ATG (reference)								
Thymoglobin vs no	0.372 (0.218-0.634)	0.000274	0.269 (0.113-0.642)	0.0031	0.587 (0.351-0.981)	0.0422	0.548 (0.26-1.16)	0.114
Grafalon vs no	0.176 (0.0935-0.333)	8.35e-08	0.2 (0.0789-0.508)	0.000711	0.68 (0.414-1.12)	0.127	0.759 (0.374-1.54)	0.444
age (per 10y)	0.888 (0.767-1.03)	0.116	0.84 (0.666-1.06)	0.141	1.13 (1-1.28)	0.0441	1.09 (0.923-1.29)	0.305
Year of Tx	1.05 (0.988-1.13)	0.112	1.04 (0.937-1.15)	0.483	1.01 (0.949-1.07)	0.834	0.985 (0.907-1.07)	0.725
status at Tx								
CR2+ vs CR1	0.769 (0.484-1.22)	0.267	0.808 (0.397-1.64)	0.556	0.602 (0.406-0.893)	0.0117	0.843 (0.505-1.41)	0.515
advanced vs CR1	1.61 (1.04-2.49)	0.0322	1.43 (0.716-2.87)	0.309	1.12 (0.717-1.76)	0.613	0.959 (0.513-1.79)	0.896
cytogenetics								
interm. vs favorable	1.43 (0.883-2.32)	0.146	1.15 (0.563-2.36)	0.699	0.944 (0.635-1.4)	0.776	0.889 (0.526-1.5)	0.659
poor vs favorable	1.02 (0.593-1.76)	0.94	1.08 (0.481-2.4)	0.86	0.665 (0.419-1.05)	0.0829	0.592 (0.314-1.12)	0.106
KPS>=90% vs <90%	0.874 (0.592-1.29)	0.497	0.985 (0.533-1.82)	0.962	1.07 (0.763-1.5)	0.692	0.839 (0.532-1.32)	0.45

Donor type								
UD 10/10 vs MSD	3.39 (2.24-5.13)	8.77e--09	2.98 (1.61-5.5)	0,0005	1.29 (0.875-1.89)	0.199	0.732 (0.424-1.26)	0.261
UD 9/10 vs MSD	2.82 (1.54-5.18)	0.000808	4.96 (2.15-11.4)	0.000173	1.52 (0.915-2.52)	0.106	1.02 (0.488-2.14)	0.956
PB vs BM	1.02 (0.664-1.56)	0.936	1.46 (0.727-2.94)	0.288	0.977 (0.685-1.39)	0.899	1.39 (0.84-2.31)	0.199
F->M vs other	1.06 (0.716-1.57)	0.767	1.06 (0.584-1.94)	0.84	1.41 (1.03-1.93)	0.0339	1.35 (0.89-2.04)	0.159
Pat. CMV pos vs neg	0.932 (0.669-1.3)	0.679	1.37 (0.803-2.36)	0.246	1.08 (0.817-1.42)	0.595	1.3 (0.88-1.92)	0.187
Don. CMV pos vs neg.	1.22 (0.879-1.69)	0.236	1.54 (0.915-2.58)	0.104	1.02 (0.776-1.34)	0.886	0.79 (0.539-1.16)	0.228
FluTBI vs CyTBI	0.705 (0.351-1.42)	0.327	0.446 (0.13-1.52)	0.198	1.27 (0.757-2.14)	0.364	1.99 (1.01-3.95)	0.0482
center (frailty)		0.00877		0.211		0.00765		0.000165

Supplementary table S2: Detailed description of other causes of death.

no ATG group	N=9
Pulmonary toxicity	2
MOF	1
renal failure	1
Thrombotic Microangiopathy	1
GI toxicity	1
Liver failure	1
lymphoproliferative disorder	1
progressive multiple leukoencephalopathy due to rituximab (GVHD treatment)	1

ATG group	N=11
MOF	4
toxic ARDS	2
Pulmonary hypertension after pulmonary embolism; suspicion of a seizure or syncope with aspiration	1
PTLD treated with Rituximab	1
Liver toxicity	1
Lymphoproliferative disorder	1
unknown	1
Total	11

EBMT centers who contributed cases for this study.

2008-2016	N
515 Helsinki [Univ Central H]	44
209 Leuven [Univ H]	37
234 Brussels [St. Luc]	33
246 Rotterdam [Erasmus MC]	31
556 Budapest [National Med Ctr]	30
666 Villejuif [Gustave Roussy]	23
726 Liege [University]	21
387 Birmingham [Queen Elizabeth]	19
744 Gent [Univ H]	15
996 Antwerp_Edegem [UZA]	15
225 Turku [University]	14
259 Essen [Univ H]	14
671 Lyon [H E Herriot]	14
252 Creteil [H Mondor Hematol]	13
389 Leipzig [Univ, Haemat/Oncol]	13
260 Barcelona [SCreu i S Pau]	12
614 Hamburg [Univ H]	12
661 Rennes [H Sud/Pontchaillou]	12
397 Riyadh [King Faisal]	11
625 Nuernberg [Klinikum]	11
262 Paris [Pitie-Salpetriere]	10
283 Lund [Univ H]	10
623 Verona [Policlinico]	10
145 Stuttgart [Robert_Bosch_Kh]	9
294 Milano [Osp Niguarda]	9
680 Muenster [University]	9
257 Dublin [St James]	8
656 Prague [Ist Hematology]	8
717 Nottingham [City H]	8
941 Rouen [Becquerel]	8
208 Zürich [208]	7
214 Barcelona [H Clinic]	7
295 Hannover [Medical Univ]	7
759 Barcelona [H Univ Bellvitge]	7
206 Copenhagen [Rigshospitalet]	6
250 Saint_Etienne [St Etienne]	6
807 Berlin [Charité Univ]	6
202 Basel [202]	5

215 Brussels [Jules Bordet]	5
264 Poitiers [H La Miletrie]	5
277 Lille [H Claude Huriez]	5
775 Paris [St Antoine]	5
931 Suzhou [First Soochow]	5
205 London [Hammersmith]	4
224 London [UCL]	4
251 Caen [Hopital, Hematol]	4
261 Geneva [261]	4
272 Tours [H Bretonneau]	4
409 Petach-Tikva [Beilinson H]	4
580 Amman [King Hussein]	4
704 Southampton [General H]	4
778 Sheffield [Royal Hallamshire]	4
786 Mainz [Johannes-Gutenberg]	4
217 Genova [S Martino]	3
255 Oxford [Radcliffe H]	3
268 Belfast [City H]	3
270 Grenoble [H A Michallon]	3
297 Frankfurt am Main [Goethe-Univ]	3
308 Graz [Medical Univ]	3
428 Gliwice [Sklodowska]	3
533 Jena [Friedrich-Schiller]	3
546 Groningen [Univ H]	3
665 Clamart [H Percy]	3
713 Leicester [Royal Infirmary]	3
768 London [S Bartholomew`s]	3
994 Istanbul [Nightingale]	3
160 Paris [H Necker]	2
218 London [Royal Marsden]	2
223 Tuebingen [Univ]	2
233 Besancon [H Jean Minjoz]	2
239 Utrecht [University]	2
240 Bologna [S Orsola-Malpighi]	2
254 Leeds [St James]	2
258 Jerusalem [Univ Hadassah]	2
286 Pavia [S Matteo]	2
338 Halle [Univ Martin-Luther]	2
348 Aachen [RWTH]	2
359 Magdeburg [vGuericke U]	2
513 Munich [Kl Grosshadern]	2

524 Heidelberg [Medizinische Kl]	2
606 Cuneo [S Croce e Carle]	2
624 Toulouse [H Purpan]	2
650 Angers [CHRU]	2
658 Bergamo [Ospedale, ematol]	2
672 Strasbourg [H Hautepierre]	2
780 Manchester [Christie]	2
787 Regensburg [University]	2
808 Dresden [Universitaets Kl]	2
141 Brescia [Civili, Adulti]	1
142 Mannheim [Univ]	1
152 Augsburg [Zentral Kl]	1
153 Hamburg [AK St Georg]	1
207 Paris [St Louis]	1
212 Stockholm [Univ H]	1
227 Vienna [Medizinische Univ]	1
231 Torino [S. Giovanni (CTO)]	1
232 Rome [Emat, La Sapienza]	1
237 Nijmegen [St Radboud]	1
238 Córdoba [Reina Sofia]	1
244 Glasgow [Royal Infirmary]	1
248 Pescara [Osp Civile]	1
253 Nantes [Hotel Dieu]	1
265 Milano [Osp Maggiore]	1
289 Goeteborg [Sahlgrenska Univ H]	1
303 Cardiff [Univ Wales]	1
311 Wiesbaden [Kl Diagnostik]	1
386 Bristol [Royal H Sick Chil]	1
444 Riyadh [Aziz]	1
506 Brugge [AZ Sint-Jan]	1
523 Nice [H de l`ARCHET I]	1
526 San_Giovanni_Rotondo [IRCCS]	1
544 Monza [Osp S Gerardo]	1
553 Krakow [Jagiellonian Univ]	1
566 Cambridge [Addenbrookes H]	1
577 Pamplona [H de Navarra]	1
584 Barcelona [V d`Hebron Adults]	1
592 Idar-Oberstein [Kl Knochenmarktr]	1
594 Linz [Elisabethinen H]	1
597 Brno [Univ H]	1
601 Manchester [Royal Infirmary]	1

613 Barcelona [H Trias i Pujol]	1
617 Ankara [Ibni Sina H]	1
634 Aarhus [Univ, Hematol]	1
676 Vandoeuvre_Les_Nancy [H d`Enfants]	1
677 Katowice [Silesian Med Acad]	1
693 Warsaw [Inst Haematology]	1
729 Hradec_Králové [Charles U H, Hem]	1
754 Tel-Hashomer [Univ Adults]	1
858 Jeddah [King Faisal]	1
926 Montpellier [University]	1
Total	724