22 OTTOBRE 2020

5 NOVEMBRE 2020

20 GENNAIO 2021

CONDIVISIONE

Incontri di esperienze e punti di vista sulla terapia di condizionamento pre-HSCT

Treo10, Treo12, Treo14 : razionale e risultati a confronto

Francesco Onida

Treosulfan in conditioning for allo-HCST: where did we start from?

Treosulfan and fludarabine: a new toxicity-reduced conditioning regimen for allogeneic hematopoietic stem cell transplantation

Jochen Casper, Wolfgang Knauf, Thomas Kiefer, Daniel Wolff, Beate Steiner, Ulrich Hammer, Rudolf Wegener, Hans-Dieter Kleine, Stefan Wilhelm, Agnes Knopp, Gernot Hartung, Gottfried Dölken, and Mathias Freund

30 pts (03/1999-01/2002) **not eligible for standard MAC** (autograft, epatotoxicity, age, aspergillosis, poor lung function…)

Treo 10 g/m^2 x 3 (-6 to -4) /Fluda 30 mg/m^2 x 5 (-6 to -2) + ATG 10 mg/kg x 3 days in MUD (-4 to -2)

Median age 49 yrs (20-60); DX: AML, MDS, CML, MM, CLL, NHL

14 HLA-matched related /16 MUD

Prompt Neutr & PLT engraftment in 100%

Casper J et al. Blood 2004;103:725-731

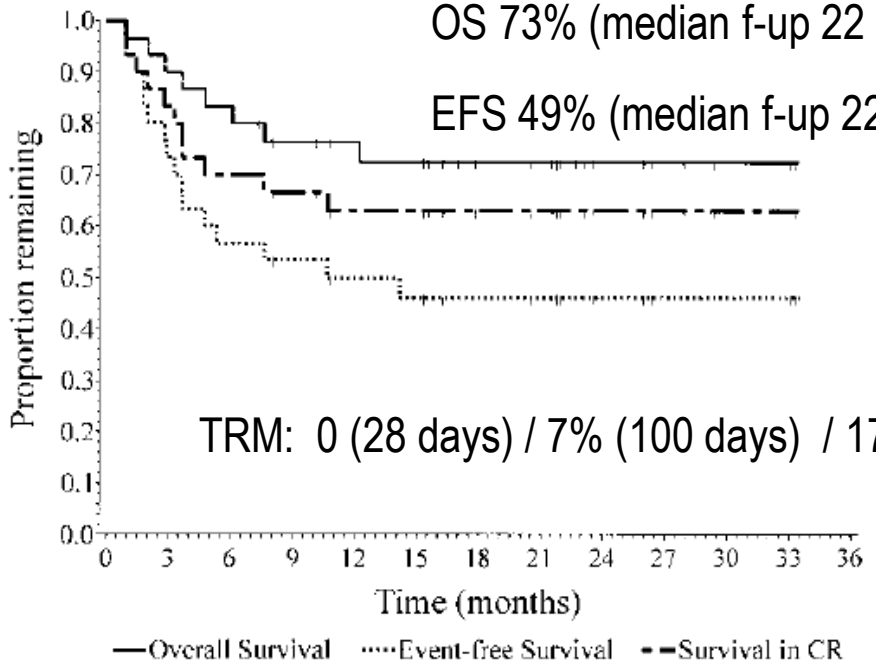
Treo10/Flu150: Results

Table 2. Number of patients having nonhematologic toxicity after treosulfan and fludarabine conditioning

	CTC grade (%)				
	0	1	2	3	4
Nausea	5 (17)	17 (57)	8 (27)	0	0
Vomiting	9 (30)	11 (37)	9 (30)	1 (3)	0
Mucositis	10 (33)	14 (47)	6 (20)	0	0
Creatinine	14 (43)	10 (33)	6 (20)	0	0
ALT/AST	2 (7)	9 (30)	9 (30)	10 (33)	0
Bilirubin	9 (30)	11 (37)	5 (17)	4 (13)	1 (3)
Alkaline phosphatase	13 (43)	13 (43)	4 (13)	0	0
Diarrhea	11 (37)	9 (30)	7 (23)	3 (10)	0
Constipation	20 (67)	1 (3)	8 (27)	1 (3)	0
Fever without neutropenia	14 (43)	9 (30)	5 (17)	1 (3)	1 (3)
Fever with neutropenia	14 (43)	0	0	16 (57)	0
Infection	6 (20)	0	0	22 (73)	2 (7)
Confusion	28 (94)	0	1 (3)	1 (3)	0
Polyneuropathy, sensory	26 (87)	3 (10)	0	1 (3)	0
Polyneuropathy, motor	29 (97)	0	0	1 (3)	0
Pain	9 (30)	6 (20)	15 (50)	0	0

Table 3. Number of patients having acute and chronic GVHD (excluding patients with GVHD after DLI)

	All patients (%)	MRD (%)	MUD (%)
Acute, n = 30			
0	13 (43)	7 (50)	6 (38)
I	8 (27)	3 (21)	5 (31)
II	5 (17)	2 (14)	3 (19)
III	2 (7)	1 (7)	1 (6)
IV	2 (7)	1 (7)	1 (6)
Chronic, n = 26			
None	16 (62)	7 (58)	9 (64)
Limited	2 (8)	1 (7)	1 (6)
Extensive	8 (31)	4 (33)	4 (29)



OS 73% (median f-up 22 months)

EFS 49% (median f-up 22 months)

TRM: 0 (28 days) / 7% (100 days) / 17% (1 yr)

Casper J et al. Blood 2004;103:725-731

Dose-escalated treosulphan in combination with cyclophosphamide as a new preparative regimen for allogeneic haematopoietic stem cell transplantation in patients with an increased risk for regimen-related complications

DW Beelen[1], R Trenschel[1], J Casper[2], M Freund[2], RA Hilger[3], ME Scheulen[3], N Basara[4], AA Fauser[4], B Hertenstein[5], HA Mylius[6], J Baumgart[6], U Pichlmeier[6], JR Hahn[7] and E Holler[7]

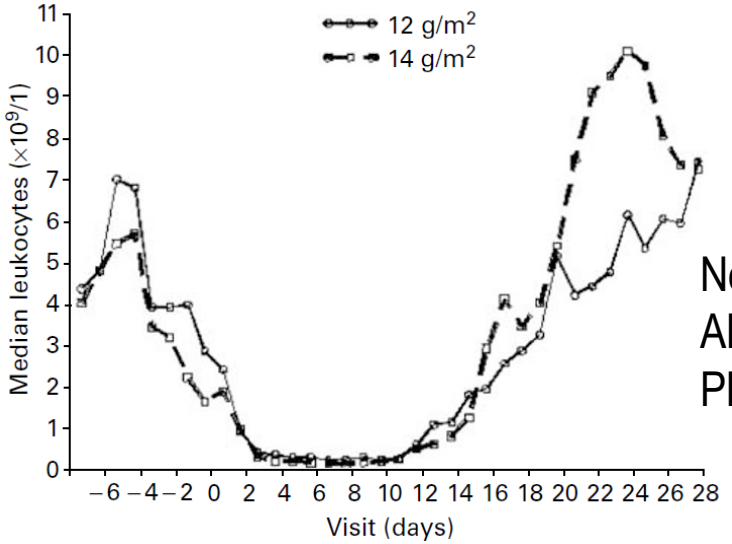
18 pts (07/2000-04/2002) **not eligible for standard MAC**

- Treo 12 or 14 g/m^2 x 3 (-6 to -4) [total dose 36 – 42 g/m^2]

- CTX 60 mg/kg x 2 (-3 to -2)

Median age 44 yrs (19-64); DX: AML, ALL, MDS, CML, NHL

Donor HLA-id Sib in all pts



Neutropenia 9 days
ANC >1000: 16 (11-25)
PLT >20: 16 (11-57)

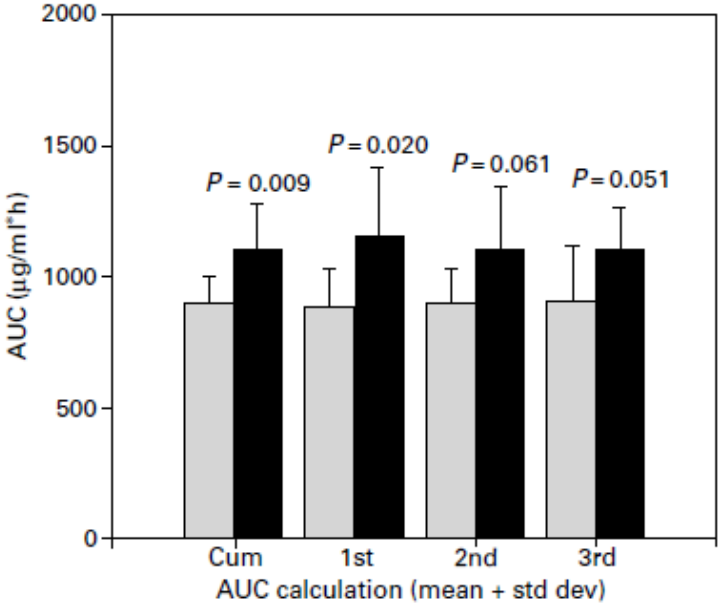
Table 2 Summary of study patient characteristics

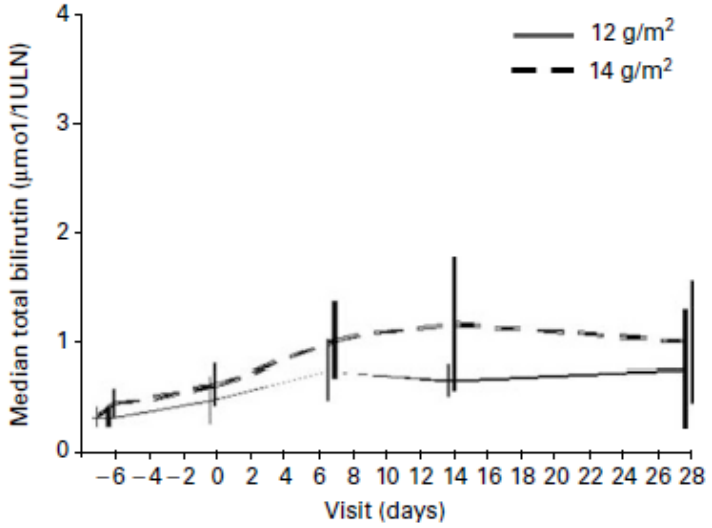
	Treosulphan dose level	
Patient number	*12 g/m² n = 8*	*14 g/m² n = 10*
Median age, years (range)	40 (19–59)	51 (23–64)
Male/female	7/1	3/7
Median donor age, years (range)	38 (20–62)	48 (16–56)
Gender match, n		
Female to male	3	2
Other	5	8
Median CD34$^+$ cell dose × 10^6 per kg recipient body weight (range)	6.8 (3.3–22.4)	3.9 (1.0–8.4)
Indications for transplantation, n		
MDS/sMDS	0/0	1/1
AML/sAML	1/1	2/2
ALL	4	3
CML	1	1
T-NHL	1	0
Median time to Tx, months (range)	6 (3–106)	6 (3–100)

Beelen DW et al. BMT 2005;35:233-241

Treo10-12+CTX: Results

	Treosulphan 3 × 12 g/m² (n = 8)	*Treosulphan 3 × 14 g/m² (n = 10)*	*P*
AUC, μg/ml*h (1st dose)	898 ± 104	1104 ± 173	<0.01
C_{max}, μg/ml	260 ± 35	322 ± 47	<0.01
Terminal half life, h	2.1 ± 0.5	2.0 ± 0.6	NS
CL_{total}, ml/min	225 ± 23	216 ± 32	NS
Vss, l	34 ± 5	31 ± 7	NS
Renal excretion, % of total dose	39 ± 5	39 ± 7	NS



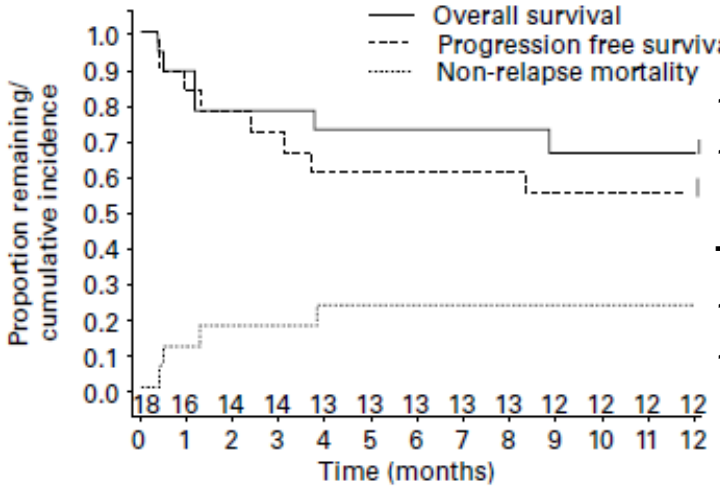


	Regimen-related adverse events (%)		
Treosulphan dose, g/m² / *Patient number*	*3 × 12 n = 8*	*3 × 14 n = 10*	*Total n = 18*
Allergy/immunology	—	—	—
Cardiovascular (arrhythmia)	1 (13)	2 (20)	3 (17)
Cardiovascular (general)	—	2 (20)	2 (11)
Coagulation	—	—	—
Constitutional symptoms	1 (13)	1 (10)	2 (11)
Dermatology/skin	1 (13)	1 (10)	2 (11)
Gastrointestinal	2 (25)	5 (50)	7 (39)
Haemorrhage	—	2 (20)	2 (11)
Hepatic	4 (50)	3 (30)	7 (39)
Infection/febrile neutropenia	5 (63)	5 (50)	10 (56)
Metabolic/laboratory	—	2 (20)	2 (11)
Neurology	—	—	—
Pain	1 (13)	2 (20)	3 (17)
Pulmonary	—	1 (10)	1 (6)
Renal/genitourinary	1 (13)	—	1 (6)
Multiorgan failure	—	—	—

Grade II-IV aGvHD 22%
Cumulative cGvHD 33%

Treo 12 vs 14: NO DIFF!

NRM 1 yr 22% (Treo12 =13% /14=30% NS)



1 yr OS 67%
1 yr PFS 56%

Treo12 vs 14
1 yr OS 75% vs 60%
1 yr PFS 50% vs 60%

Beelen DW et al. BMT 2005;35:233-241

Allogeneic Hematopoietic Stem-Cell Transplantation in Patients With Hematologic Malignancies After Dose-Escalated Treosulfan/Fludarabine Conditioning

Jochen Casper, Daniel Wolff, Wolfgang Knauf, Igor W. Blau, Tapani Ruutu, Liisa Volin, Hannes Wandt, Kerstin Schäfer-Eckart, Jerzy Holowiecki, Sebastian Giebel, Johan Aschan, Axel R. Zander, Nicolaus Kröger, Inken Hilgendorf, Joachim Baumgart, Heidrun A. Mylius, Uwe Pichlmeier, and Mathias Freund

55 pts (12/2001-06/2003) **not eligible for standard MAC**

- Treo 10 (n=20) or 12 (n=18) or 14 (n=17) g/m^2 x 3 (-6 to -4)

- Fludarabine 30 mg/m2 x 5 (-6 to -2) + ATG 2 mg/kg in MUD (-3 to -1)

Median age 50 yrs (18-66); DX: AML, MDS, CML, CLL, NHL

MRD in 47% / MUD in 51% / MMRD 2%

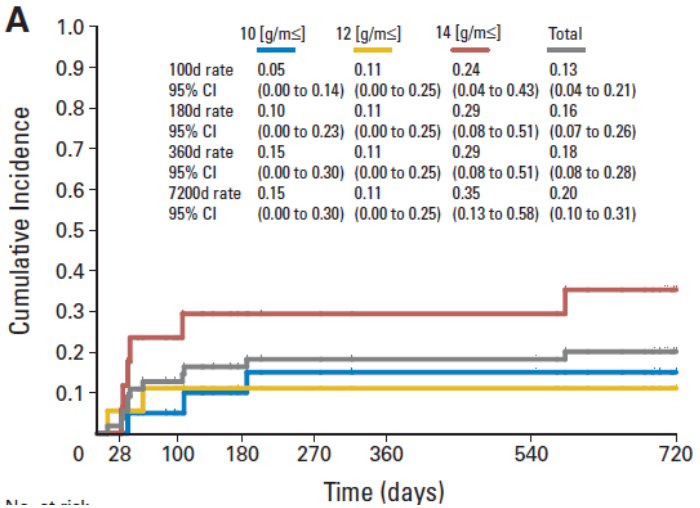
Table 2. Frequency Greater Than 5% of All Nonhematologic, NCI CTCAE Grades 3 to 4 Adverse Events Between Days −6 and +28

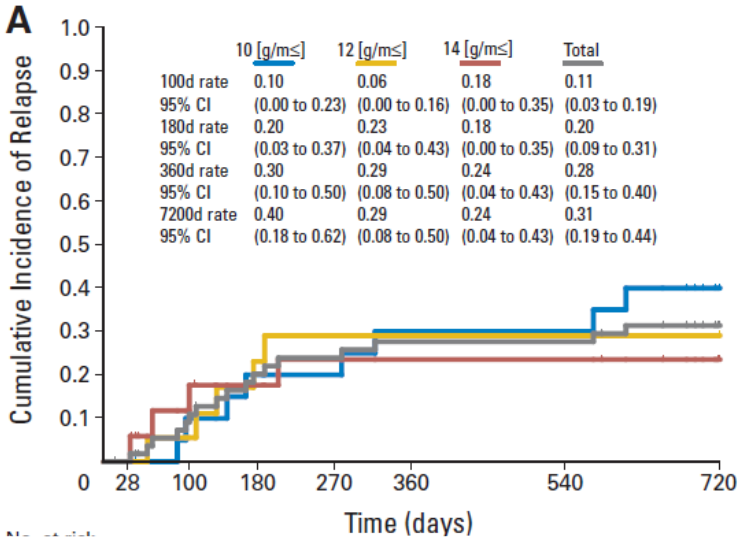
	Treosulfan Dose Group							
	3 × 10 g/m^2 (n = 20)		3 × 12 g/m^2 (n = 18)		3 × 14 g/m^2 (n = 17)		Overall (n = 55)	
Event NCI CTCAE Term	No.	%	No.	%	No.	%	No.	%
Any	18	90	12	67	13	76	43	78
Cardiac dysrhythmia	0	0	3	17	2	12	5	9
Cardiac general	2	10	1	6	2	12	5	9
Coagulation/PTT	0	0	2	11	3	18	5	9
Constitutional symptoms	0	0	1	6	3	18	4	7
Gastrointestinal	4	20	2	11	1	6	7	13
Diarrhea	3	15	0	0	0	0	3	5
Mucositis/stomatitis	1	5	1	6	1	6	3	5
Hemorrhage/bleeding	1	5	0	0	2	12	3	5
Infection	12	60	9	50	9	53	30	55
Metabolic/laboratory	13	65	10	56	9	53	32	58
ALT	7	35	5	28	4	24	16	29
AST	3	15	4	22	2	12	9	16
γ-GT	7	35	7	39	6	35	20	36
Alkaline phosphatase	2	10	2	11	0	0	4	7
Hyperbilirubinemia	1	5	1	6	2	12	4	7
Hyperglycemia	4	20	1	6	1	6	6	11
Neurology	1	5	1	6	3	18	5	9
Pulmonary	0		1	6	3	18	4	7
Renal failure	1	5	2	11	3	18	6	11

Casper J et al. JCO 2010;28:3344-3351

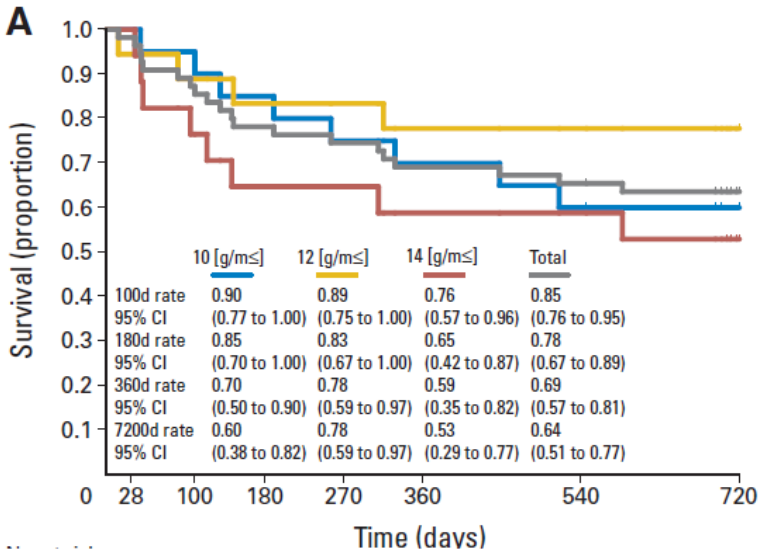
Treo10-12-14/Fluda: Results

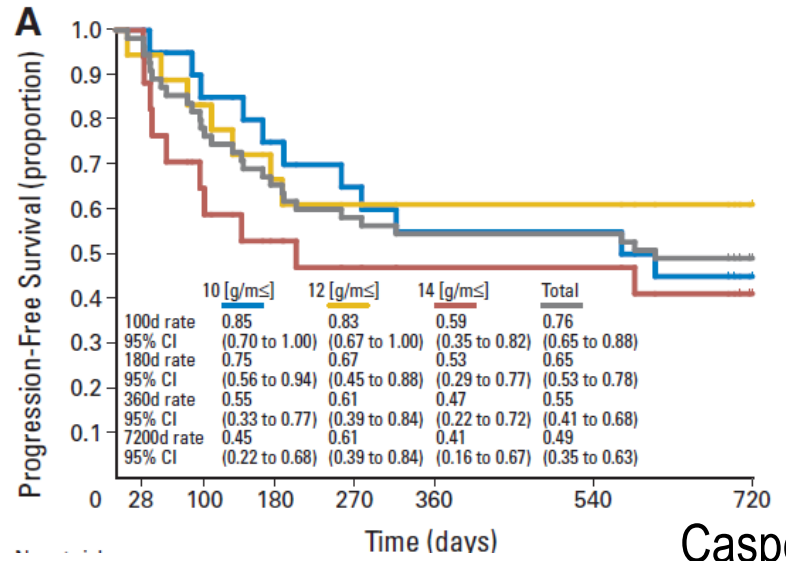
TRM: 13% (100 days) / 18% (1 yr) / 20% (2 yrs)





Grade II-IV aGvHD 42% (III-IV 5%)
Cumulative cGvHD 57% : extens = 41% vs 20% vs 0% but with higher frequency of MUD in Treo14 (with ATG)





2 yr OS 64%
2 yr PFS 49%

Treo10 vs 12 vs 14
2 yr OS 60% vs 78% vs 53%
2 yr PFS: NS differences

Casper J et al. JCO 2010;28:3344-3351

ORIGINAL ARTICLE

Allogeneic hematopoietic SCT in patients with AML following treosulfan/fludarabine conditioning

J Casper[1,12], J Holowiecki[2,13], R Trenschel[3], H Wandt[4], K Schaefer-Eckart[4], T Ruutu[5], L Volin[5], H Einsele[6], G Stuhler[6], L Uharek[7], I Blau[7], M Bornhaeuser[8], AR Zander[9], K Larsson[10], M Markiewicz[2], S Giebel[2,13], T Kruzel[2], HA Mylius[11], J Baumgart[11], U Pichlmeier[11], M Freund[1] and DW Beelen[3]

75 pts (09/2004-10/2006) **with AML in CR (80% 1CR)**

Treo 14 g/m^2 x 3 (-6 to -4) / Fluda 30 mg/m^2 x 5 (-6 to -2)

Median age 45 yrs (19-59)

HLA-id Sib donor 40% / MUD 60%

Day 28 engraftment for ANC and PLT: 93%

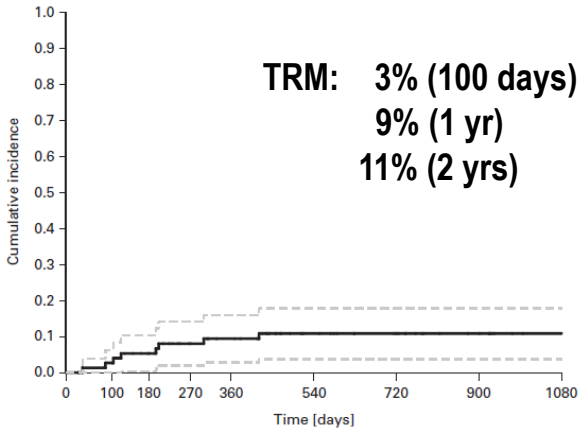
ANC >1000: 20 (12-38)
PLT >20: 14 (7-31)
Complete D chimerism: 72% day +28 → 92% day 100

Table 2. Frequencies of all CTCAE grade III-IV adverse events between day −6 and day +28

CTCAE category/term	*Worst CTCAE grade (N = 75)*		
	III N (%)	*IV N (%)*	*Total III/IV N (%)*
No. of patients with any event[a]	47 (63)	2 (3)	49 (65)
Infection total	**43 (57)**	**1 (1)**	**44 (59)**
Febrile neutropenia	30 (40)	0 (0)	30 (40)
Infection with grade III/IV neutrophils	14 (19)	1 (1)	15 (20)
Infection with normal or grade I/II ANC	4 (5)	0 (0)	4 (5)
Infection - Other	3 (4)	0 (0)	3 (4)
Infection with unknown ANC	1 (1)	0 (0)	1 (1)
Gastrointestinal total	**5 (7)**	**0 (0)**	**5 (7)**
Mucositis/stomatitis (clinical examination)	4 (5)	0 (0)	4 (5)
Nausea	2 (3)	0 (0)	2 (3)
Gastrointestinal - other	1 (1)	0 (0)	1 (1)
Constitutional symptoms	**3 (4)**	**0 (0)**	**3 (4)**
Pain	**3 (4)**	**0 (0)**	**3 (4)**
Pulmonary/upper respiratory	**3 (4)**	**0 (0)**	**3 (4)**
Blood/BM	**1 (1)**	**1 (1)**	**2 (3)**
Renal/genitourinary	**1 (1)**	**1 (1)**	**2 (3)**
Coagulation	**1 (1)**	**0 (0)**	**1 (1)**
Dermatology/skin	**1 (1)**	**0 (0)**	**1 (1)**
Endocrine	**1 (1)**	**0 (0)**	**1 (1)**
Hemorrhage/bleeding	**1 (1)**	**0 (0)**	**1 (1)**
Neurology	**1 (1)**	**0 (0)**	**1 (1)**

Table 3. Frequencies of CTCAE grades III-IV nonhematologic laboratory changes up to day +28

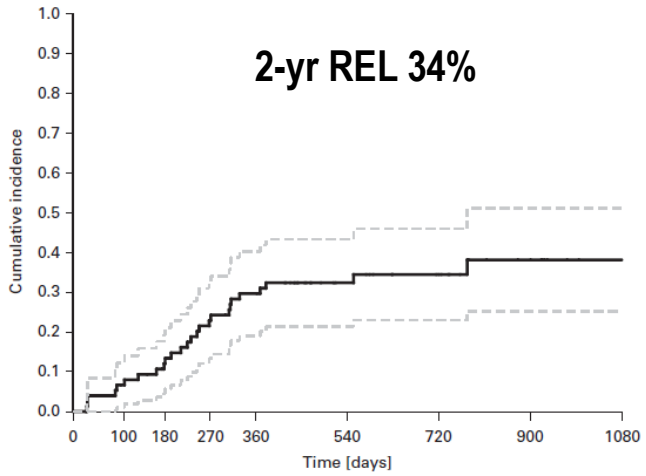
Laboratory parameter	*Worst CTCAE grade (N = 75)*		
	III N (%)	*IV N (%)*	*Total III/IV N (%)*
ALT	10 (13)	0 (0)	10 (13)
AST	1 (1)	0 (0)	1 (1)
Gamma-GT	14 (19)	1 (1)	15 (20)
Alkaline phosphatase	1 (1)	0 (0)	1 (1)
Bilirubin	6 (8)	0 (0)	6 (8)
Hyperglycemia	1 (1)	0 (0)	1 (1)
Hypokalemia	5 (7)	1 (1)	6 (8)
Hyponatremia	1 (1)	0 (0)	1 (1)
Hypomagnesemia	1 (1)	0 (0)	1 (1)

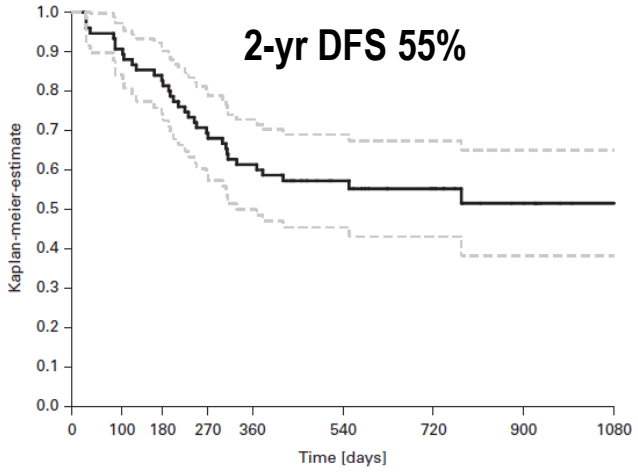


TRM: 3% (100 days)
9% (1 yr)
11% (2 yrs)

Casper J et al. BMT 2012;47:1171-1177

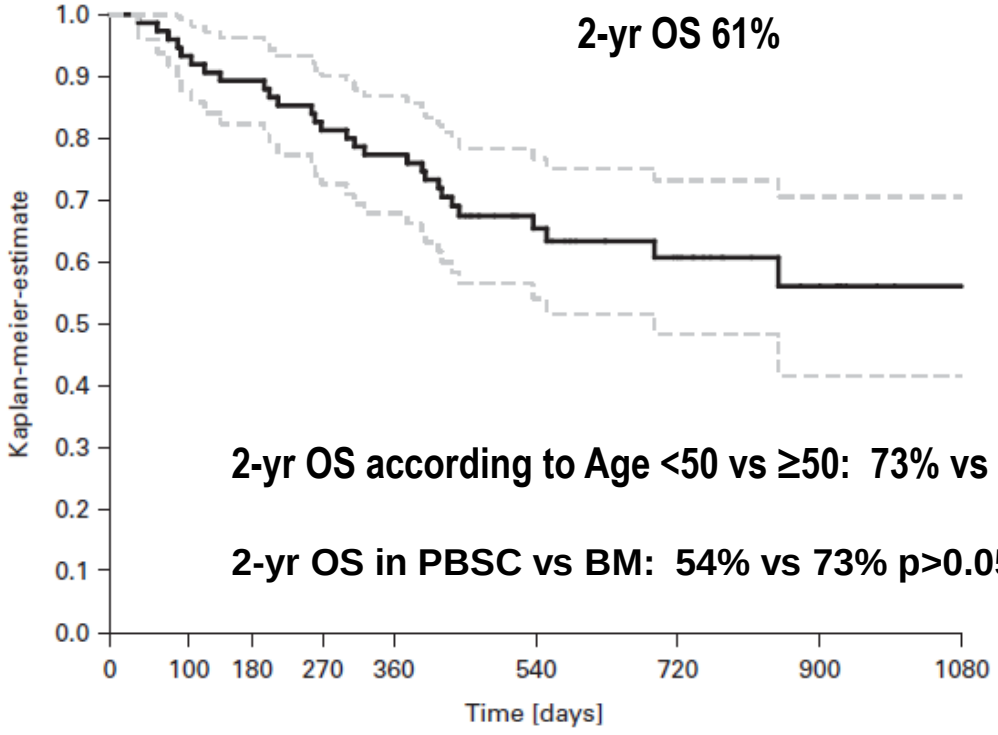
Treo14/Fluda in AML: Results





Grade II-IV aGvHD 21% (III-IV 11%)

Cumulative cGvHD = 48%
extensive = 16%



2-yr OS according to Age <50 vs ≥50: 73% vs 40% p>0.01

2-yr OS in PBSC vs BM: 54% vs 73% p>0.05

2-yr DFS according to Age <50 vs ≥50: 69% vs 32% p>0.001

Casper J et al. BMT 2012;47:1171-1177

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]

3293 pts (2000-2014)

de novo AML (2588) / sAML (705)

Median time to engraftment:

- FB4 15 days
- FB2 17 days
- FT14 17 days
- FT12 15 days

Patient Characteristics

	FB4 (n = 1533)	FB2 (n = 1457)	FT14 (n = 403)	FT12 (n = 168)	*P*
Median age, yr (range)	48 (18-74)	60 (18-77)	57 (19-73)	60 (21-73)	<.0001
Age, yr, IQR	36-56	54-64	50-63	54-65	
Gender, male	55	54	50	52	.26
Disease status					
CR1	73	74	56	52	< .0001
CR2/3	13	16	21	19	
Active disease	14	10	23	29	
Secondary AML	15	24	25	40	<.0001
Donor, sibling	62	40	36	33	<.0001
F → M	22	17	17	18	.007
Stem cell source, PBSC	85	95	90	95	<.0001
CMV status					
D–/R–	13	25	22	19	< .0001
D + /R–	7	9	6	8	
D–/R +	19	23	28	27	
D + /R +	61	43	44	46	
In vivo TCD	50	85	55	65	<.0001
Year of SCT	2012 (2000-2014)	2011 (2000-2014)	2010 (2003-2014)	2010 (2002-2014)	<.0001

Shimoni A et al. BBMT 2018;24:751-757

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3293 pts (2000-2014)

de novo AML (2588) / sAML (705)

Median time to engraftment:

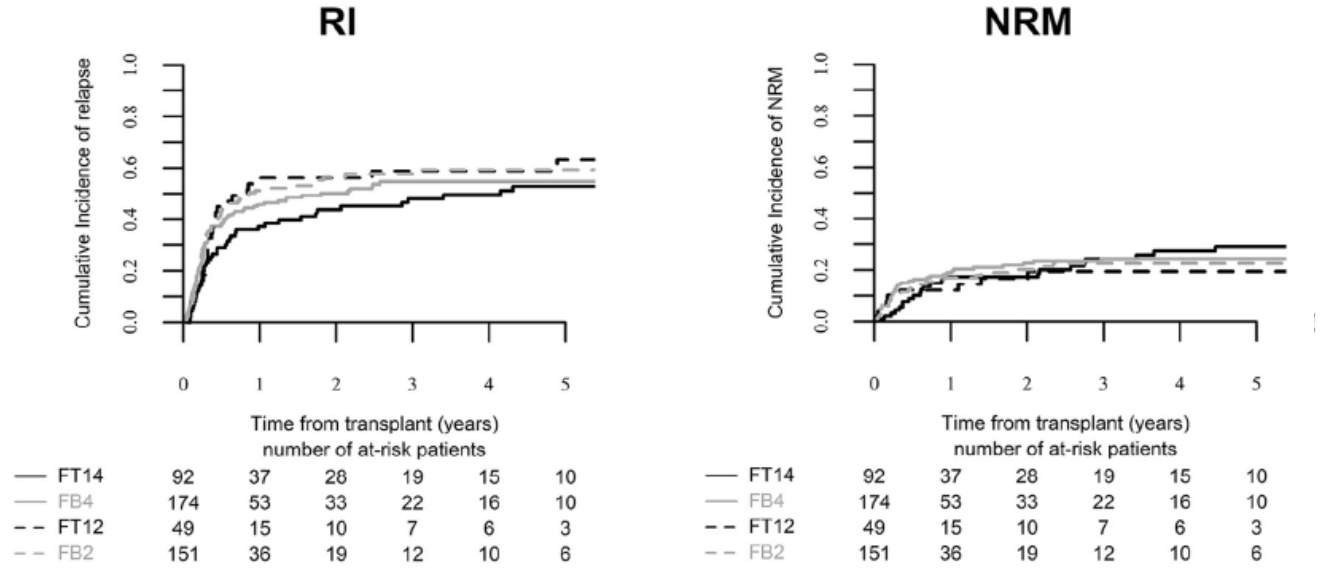
- FB4 15 days
- FB2 17 days
- FT14 17 days
- FT12 15 days

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 (.90-1.42)	.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

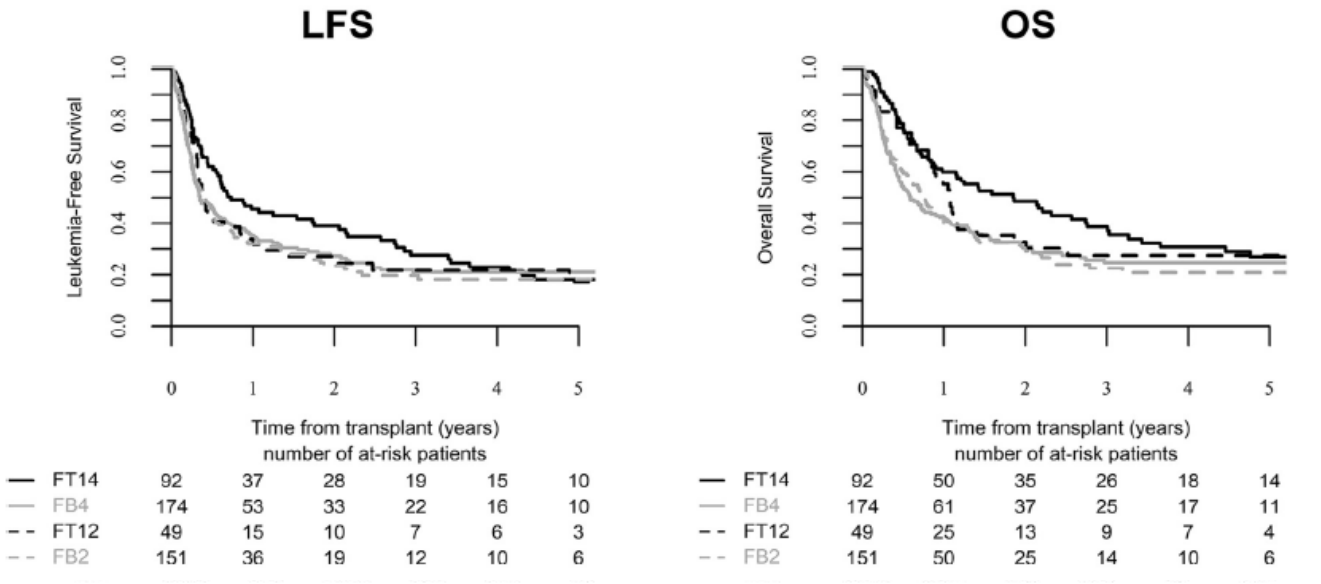
Shimoni A et al. BBMT 2018;24:751-757

EBMT ALWP BF4 vs BF2 vs FT14 vs FT12: Results



Multivariate Analysis of Factors Predicting Relapse and NRM

	Relapse		NRM	
	HR (95% CI)	P	HR (95% CI)	P
Conditioning				
FB4	1		1	
FB2	1.21 (1.02-1.43)	.03	.81 (.64-1.01)	.06
FT14	1.03 (.83-1.27)	.80	.95 (.73-1.23)	.95
FT12	1.17 (.89-1.56)	.25	.61 (.40-.94)	.02
Age per 10 yr	1.09 (1.02-1.16)	.007	1.33 (1.21-1.45)	<.0001
Gender, female	.98 (.85-1.13)	.79	.92 (.76-1.11)	.37
Disease status				
CR1	1		1	
CR2/3	1.28 (1.07-1.52)	.007	1.17 (.92-1.48)	.21
Active disease	2.44 (2.07-2.87)	<.0001	1.48 (1.17-1.89)	<.0001
Secondary AML	1.24 (1.06-1.44)	.006	1.19 (.97-1.46)	.10
Donor, unrelated	.81 (.70-.94)	.005	1.40 (1.13-1.74)	.002
F → M	1.00 (.84-1.20)	.99	1.32 (1.05-1.66)	.02
Stem cell source, PBSC	.88 (.72-1.08)	.23	1.36 (.99-1.87)	.05
Patient CMV+	.89 (.77-1.03)	.11	1.27 (1.02-1.58)	.03
Donor CMV+	.96 (.84-1.11)	.61	1.15 (.95-1.39)	.16
In vivo TCD	1.05 (.89-1.24)	.57	.80 (.64-1.00)	.06
Year of SCT	1.01 (.98-1.03)	.66	1.01 (.97-1.05)	.60

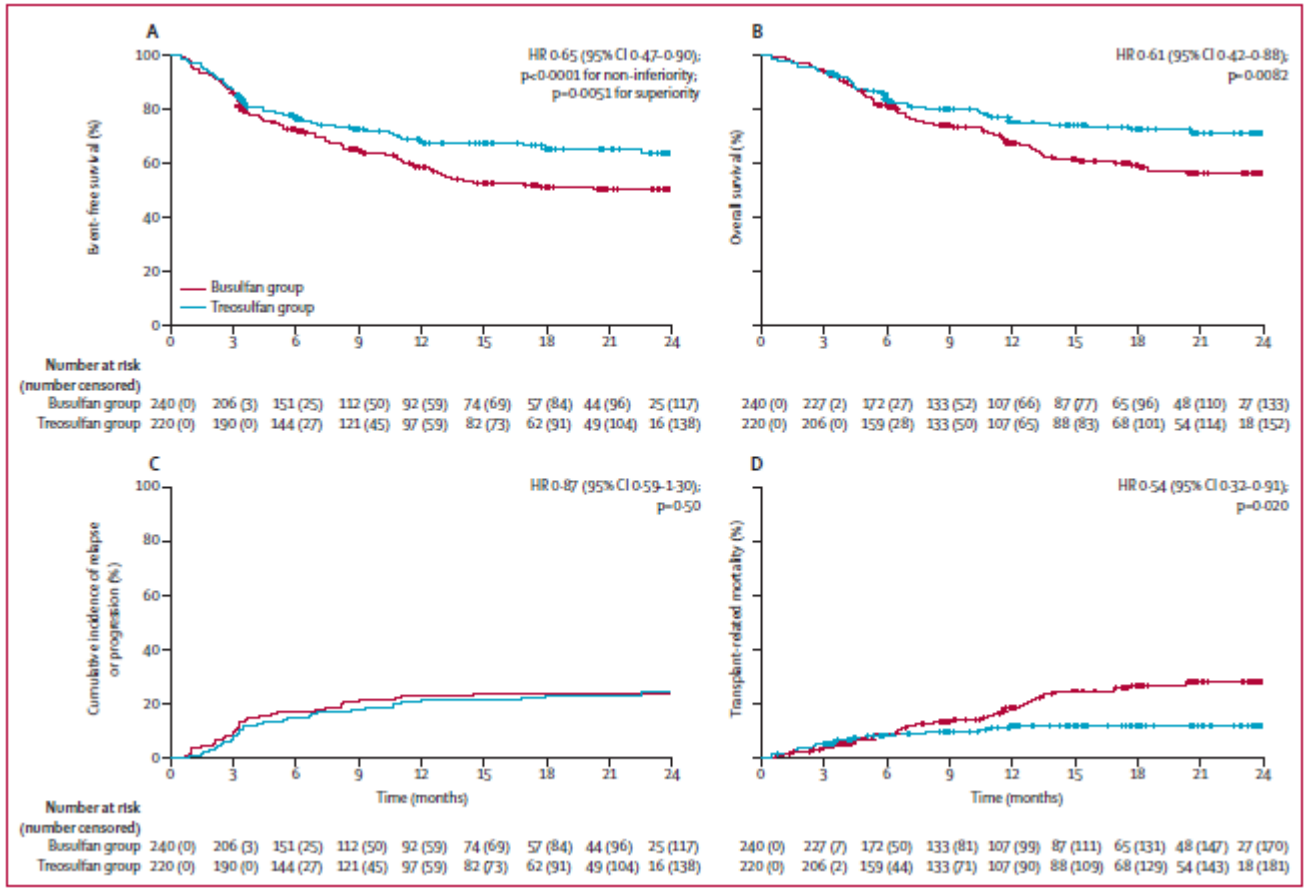


Multivariate Analysis of LFS and OS

	LFS		OS	
	HR (95% CI)	P	HR (95% CI)	P
Conditioning				
FB4	1		1	
FB2	1.04 (.90-1.19)	.63	.94 (.81-1.10)	.42
FT14	.98 (.82-1.17)	.82	.87 (.72-1.05)	.15
FT12	.99 (.78-1.27)	.96	.84 (.64-1.09)	.18
Age per 10 yr	1.14 (1.08-1.21)	<.0001	1.19 (1.11-1.26)	<.0001
Gender, female	.95 (.84-1.07)	.38	.98 (.86-1.12)	.76
Disease status				
CR1	1		1	
CR2/3	1.24 (1.07-1.44)	.005	1.15 (.98-1.36)	.09
Active disease	2.05 (1.78-2.36)	<.0001	1.97 (1.69-2.30)	<.0001
Secondary AML	1.22 (1.07-1.39)	.002	1.19 (1.04-1.37)	.01
Donor, unrelated	.99 (.87-1.12)	.83	1.09 (.95-1.26)	.21
F → M	1.09 (.94-1.27)	.25	1.10 (.94-1.30)	.24
Stem cell source, PBSC	1.01 (.84-1.21)	.91	1.02 (.84-1.25)	.82
Patient CMV+	.95 (.84-1.08)	.44	.98 (.85-1.12)	.72
Donor CMV+	1.06 (.94-1.20)	.32	1.13 (.99-1.29)	.07
In vivo TCD	.99 (.86-1.14)	.86	.97 (.84-1.13)	.73
Year of SCT	1.00 (.98-1.03)	.78	1.00 (.98-1.03)	.94

Shimoni A et al. BBMT 2018;24:751-757

Treosulfan or busulfan plus fludarabine as conditioning treatment before allogeneic haemopoietic stem cell transplantation for older patients with acute myeloid leukaemia or myelodysplastic syndrome (MC-FludT.14/L): a randomised, non-inferiority, phase 3 trial



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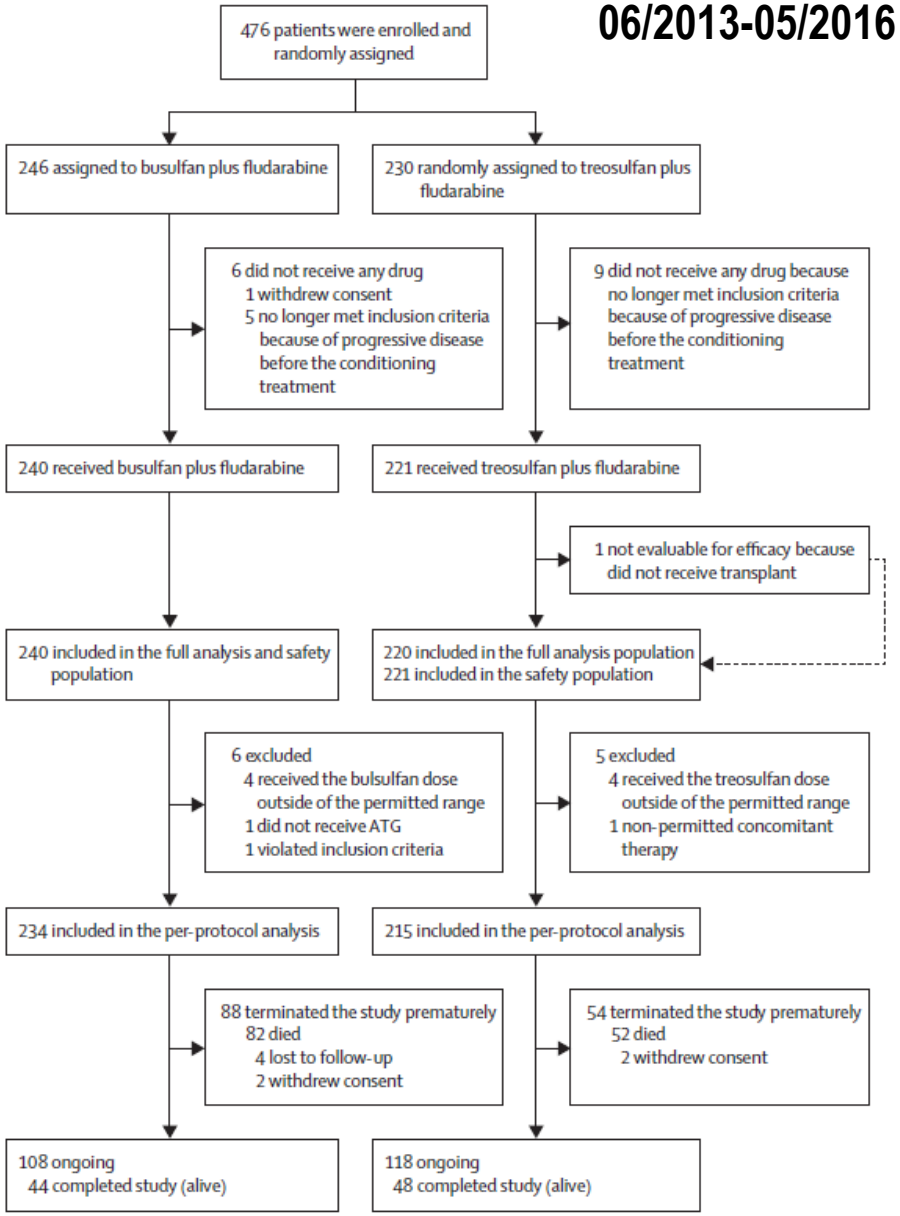

Beelen DW et al. Lancet Hematol 2020

Treo10/Flu150 vs BF2 in AML & MDS: a phase III trial

	Busulfan plus fludarabine group (n=240)	Treosulfan plus fludarabine group (n=220)	HR (95% CI)	p value
Follow-up* months	17·4 (6·3–23·4)	15·4 (8·8–23·6)	–	–
Event-free survival				
Patients with event	100 (42%)	68 (31%)	–	–
Death†	41 (17%)	23 (10%)	–	–
Relapse or progression†	51 (21%)	45 (20%)	–	–
Primary graft failure†	1 (<1%)	0	–	–
Secondary graft failure†	7 (3%)	0	–	–
24-month event-free survival (95% CI)	50·4% (42·8–57·5)	64·0% (56·0–70·9)	0·65 (0·47–0·90)	<0·0001‡ for non-inferiority; 0·0051‡ for superiority
Overall survival				
Patients with event	82 (34%)	52 (24%)	–	–
24-month overall survival (95% CI)	56·4% (48·4–63·6)	71·3% (63·6–77·6)	0·61 (0·42–0·88)	0·0082‡
Relapse or progression				
Patients with event	51 (21%)	45 (20%)	–	–
Cumulative relapse or progression incidence at 24 months (95% CI)	23·3% (17·6–29·0)	24·6% (17·8–31·3)	0·87 (0·59–1·30)	0·50§
Transplantation-related mortality				
Patients with event¶	45 (19%)	23 (10%)	–	–
GvHD	18 (8%)	10 (5%)	–	–
Haemorrhage	1 (<1%)	1 (<1%)	–	–
Renal failure	0	5 (2%)	–	–
Cardiac toxicity	4 (2%)	1 (<1%)	–	–
Interstitial pneumonitis	0	1 (<1%)	–	–
Central nervous system toxicity	1 (<1%)	0	–	–
Veno-occlusive disease or hepatic sinusoidal obstruction syndrome	1 (<1%)	0	–	–
Infection	30 (13%)	19 (9%)	–	–
Multiple organ failure	5 (2%)	5 (2%)	–	–
Other transplantation-related cause	1 (<1%)	0	–	–
Patients with event later than 6 months after transplantation¶	26 (11%)	5 (2%)	–	–
GvHD	7 (3%)	3 (1%)	–	–
Renal failure	0	1 (<1%)	–	–
Cardiac toxicity	4 (2%)	1 (<1%)	–	–
Central nervous system toxicity	1 (<1%)	0	–	–
Infection	17 (7%)	3 (1%)	–	–
Multiple organ failure	2 (1%)	1 (<1%)	–	–
24-month transplantation-related mortality (95% CI)	28·2% (21·4–36·5)	12·1% (8·1–17·7)	0·54 (0·32–0·91)	0·020‡
Non-relapse mortality				
Patients with event	41 (17%)	23 (10%)	–	–
24-month cumulative non-relapse mortality incidence (95% CI)	22·6% (16·2–28·9)	11·4% (7·0–15·9)	0·60 (0·36–1·01)	0·053§

(Table 2 continues on next page)

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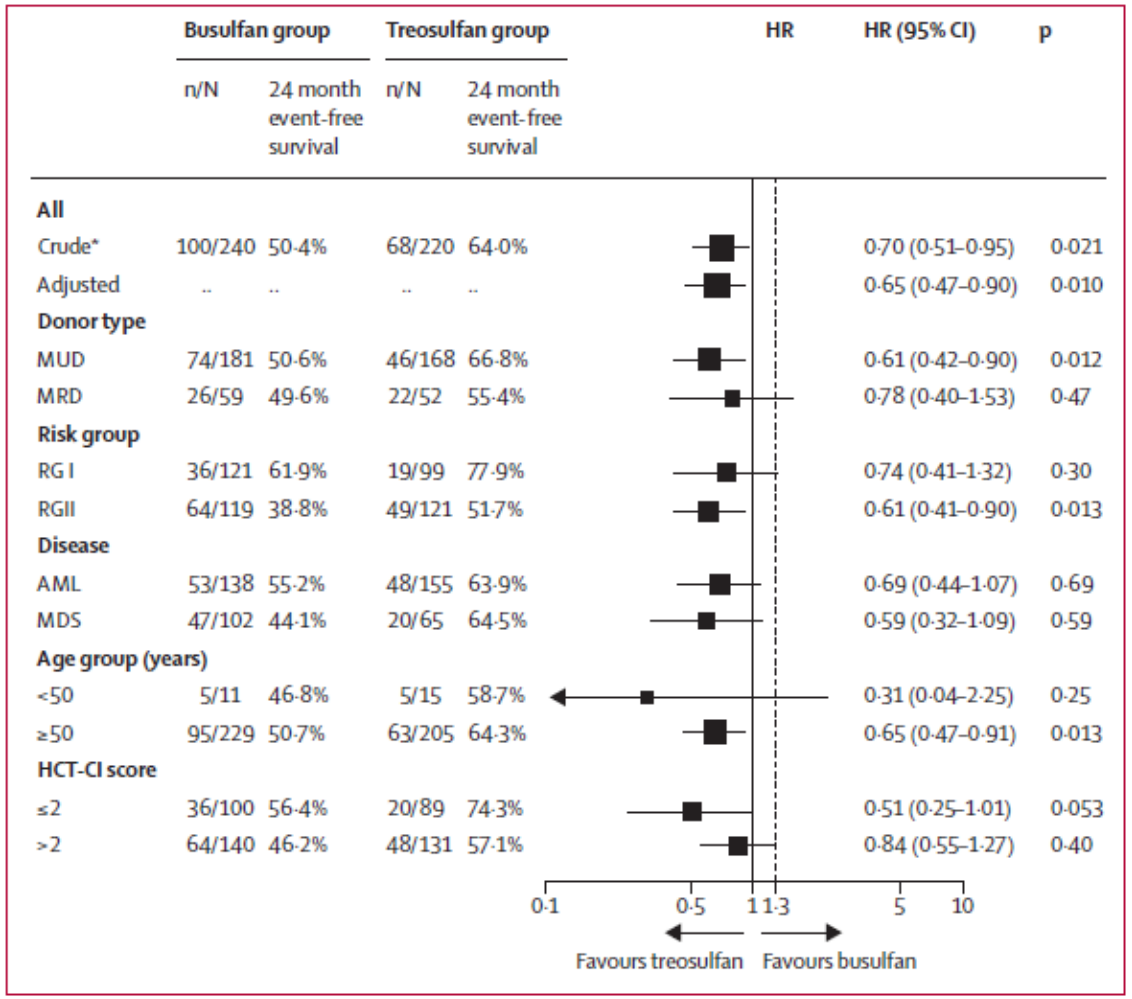
	Busulfan plus fludarabine group (n=240)	Treosulfan plus fludarabine group (n=220)	HR (95% CI)	p value
(Continued from previous page)				
Engraftment of neutrophils (>0·5 x 10⁹ cells per L)				
Patients with event	236 (98%)	217 (99%)	–	–
28-day conditional cumulative incidence of neutrophil engraftment (95% CI)	96·2% (94·1–98·3)	96·8% (93·5–100·0)	1·09 (0·92–1·28)	0·34§
Engraftment of leucocytes (>1·0 x 10⁹ cells per L)				
Patients with event	237 (99%)	217 (99%)	–	–
28-day conditional cumulative incidence of leukocyte engraftment (95% CI)	96·7% (94·3–99·0)	99·5% (96·8–100·0)	1·14 (0·97–1·34)	0·12§
Engraftment of platelets (>20 x 10⁹ cells per L)				
Patients with event	232 (97%)	215 (98%)	–	–
28-day conditional cumulative incidence of platelet engraftment (95% CI)	97·9% (96·2–99·6)	96·8% (94·2–99·3)	0·86 (0·73–1·02)	0·07§
Incidence of complete chimerism (95% CI)‖				
Day +28 visit	82·0% (76·5–86·7)	93·5% (89·3–96·4)	–	0·0080**
Day +100 visit	78·2% (72·1–83·5)	86·4% (81·0–90·8)	–	0·021**
Acute GvHD (grade 2–4)				
Patients with event	141 (59%)	114 (52%)	–	–
Cumulative incidence at 100 days (95% CI)	58·8% (52·5–65·0)	52·1% (45·5–58·7)	0·83 (0·65–1·06)	0·13††
Acute GvHD (grade 3–4)				
Patients with event	23 (10%)	14 (6%)	–	–
Cumulative incidence at 100 days (95% CI)	9·6% (5·9–13·3)	6·4% (3·2–9·6)	0·66 (0·34–1·27)	0·21††
Chronic GvHD††				
Patients with event	103/190 (54%)	91/179 (51%)	–	–
Cumulative incidence at 24 months (95% CI)	60·7% (53·1–68·4)	60·1% (49·8–70·3)	0·91 (0·69–1·20)	0·52††
Extensive chronic GvHD‡‡				
Patients with event	42/190 (22%)	28/179 (16%)	–	–
24-month cumulative incidence (95% CI)	26·1% (19·2–33·1)	18·4% (12·0–24·8)	0·68 (0·42–1·09)	0·11††

Beelen DW et al. Lancet Hematol 2020

Treo10/Flu150 vs BF2 in AML & MDS: a phase III trial



Beelen DW et al. Lancet Hematol 2020

Esperienza CTMO – Ospedale Policlinico Milano

42 pazienti trapiantati dal 01/2016 a 09/2020

Età mediana 59 anni (22-74)

Diagnosi: LMA = 24 (18 in CR, 6 con malattia)

LLA = 6 (in CR)

MDS = 3

LLC = 2

CML = 1

MDS/MPN = 2

MFI = 2

MM = 2

APLO = 15 (2 BM, 13 PBSC)

condizionamento: TTF14 = 4, TTF10 = 8, FlamsaTF10 = 1, FTMel =1, TF10 = 1

MUD = 18 (12 = 10/10, 6 = 9/10), tutti PBSC

condizionamento: TTF14 = 10, TTF10 = 2, FTMel = 1, TEC12 = 2, TF10 = 3

HLA-id SIB = 9

condizionamento: TTF14 = 6, TTF10 = 2, FlamsaTF10 = 1

VIVENTI all'ultimo F-UP = 29 (69%) – FU-mediano 18 mesi (1-57)

MORTI = 13 CAUSA di MORTE: Recidiva = 7, TRM = 5 (12%), secondo tumore = 1 (+26 mesi)

Questions?

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Un’iniziativa di

bb&c group