ANEMIA APLASTICA E TRAPIANTO DI MIDOLLO OSSEO: domande 2016

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Dichiarazione :

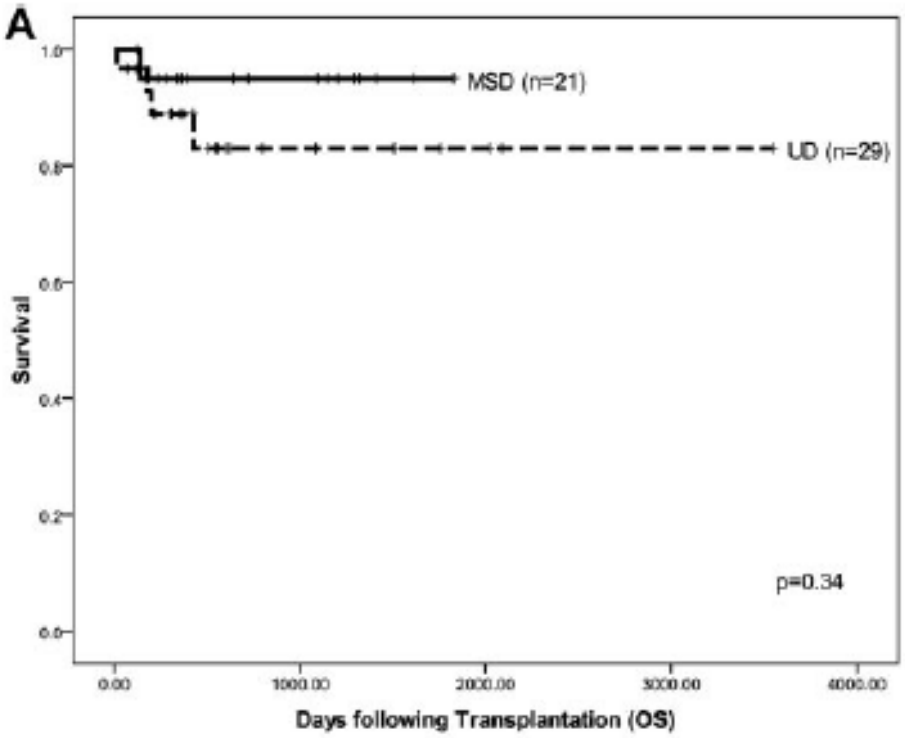
Non mi vergogno di dire “trapianto di midollo osseo”, perche’ questo e’ quello che devono ricevere pazienti con anemia aplastica

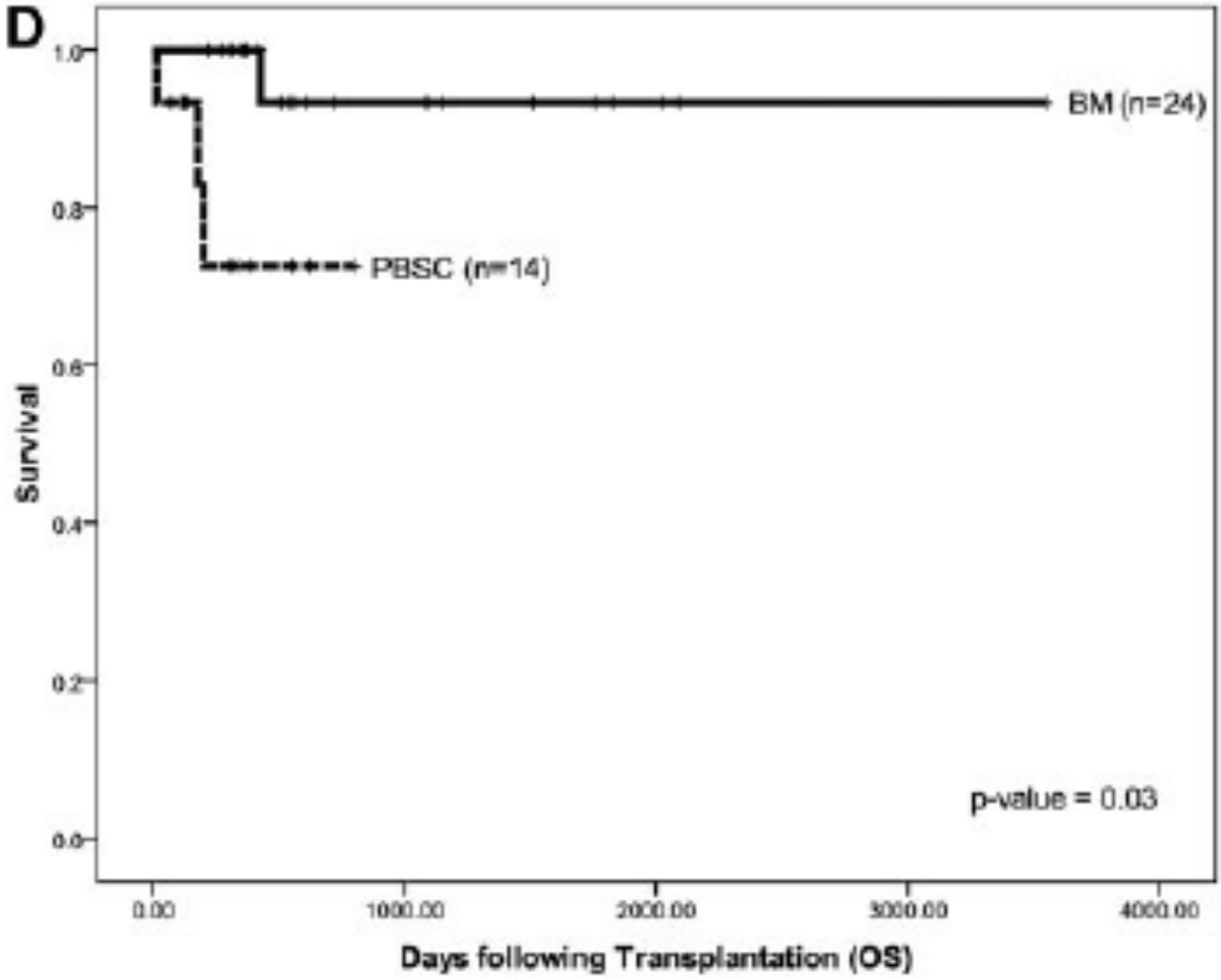
blood
2011 118: 2351-2357
doi:10.1182/blood-2010-12-327536 originally published online April 25, 2011

Alemtuzumab with fludarabine and cyclophosphamide reduces chronic graft-versus-host disease after allogeneic stem cell transplantation for acquired aplastic anemia

Judith C. Marsh, Vikas Gupta, ZiYi Lim, Aloysius Y. Ho, Robin M. Ireland, Janet Hayden, Victoria Potter, Mickey B. Koh, M. Serajul Islam, Nigel Russell, David I. Marks, Ghulam J. Mufti and Antonio Pagliuca

FCC
Fluda 30 mg /m^2 x4
CY 300 mg /m^2 x4
Campath 15 mg x4




D
1.0
0.8
0.6
0.4
0.2
0.0
Survival
BM (n=24)
PBSC (n=14)
p-value = 0.03
0.00
1000.00
2000.00
3000.00
4000.00
Days following Transplantation (OS)

bjh guideline

British Journal of Haematology, 2016, **172**, 187–207

Guidelines for the diagnosis and management of adult aplastic anaemia

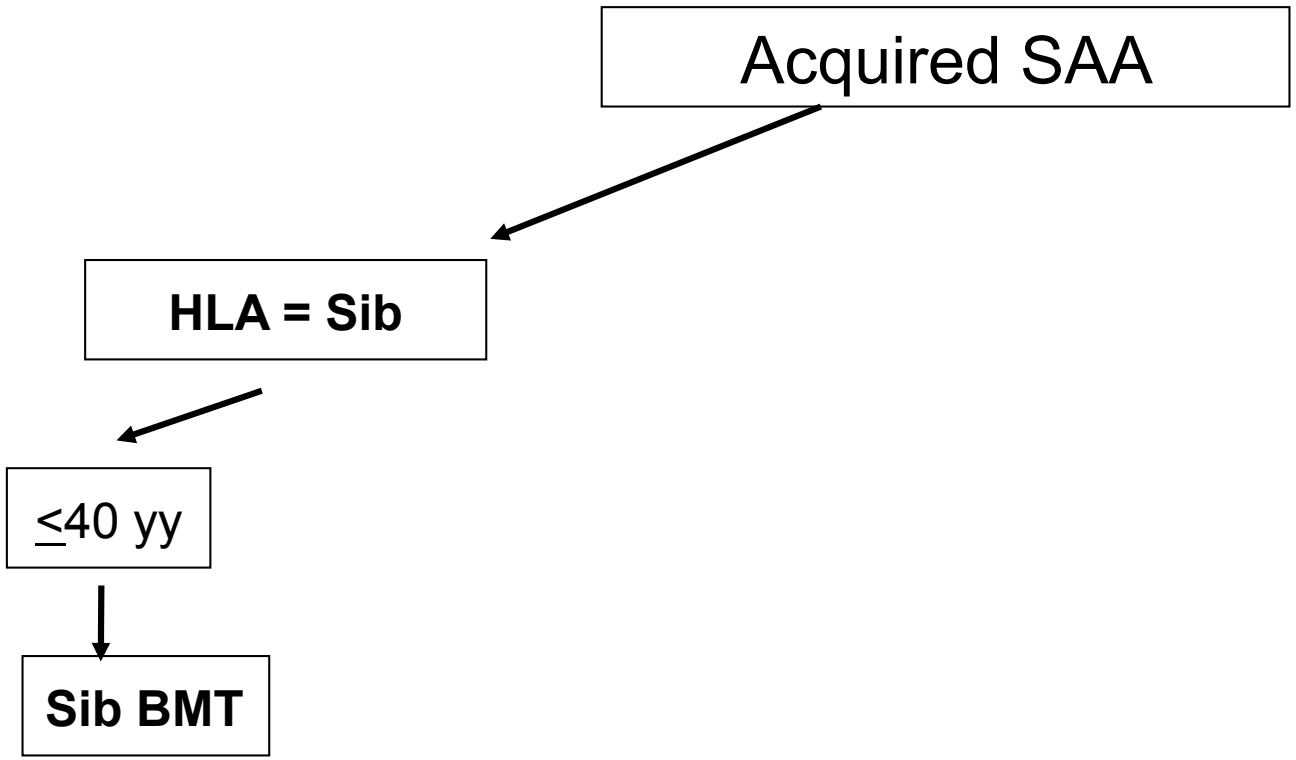
Sally B. Killick, Writing Group Chair[1] Nick Bown,[2] Jamie Cavenagh,[3] Inderjeet Dokal,[4] Theodora Foukaneli,[5] Anita Hill,[6] Peter Hillmen,[6] Robin Ireland,[7] Austin Kulasekararaj,[7] Ghulam Mufti,[7] John A. Snowden,[8] Sujith Samarasinghe,[9] Anna Wood, BCSH Task Force Member[10] and Judith C. W. Marsh[7] on behalf of the British Society for Standards in Haematology

For ATG-based conditioning regimens, BM is the preferred stem cell source (http://ebmtonline.forumservice.net; Bacigalupo *et al*, 2010). For alemtuzumab-based regimens, either BM or PBSC may be used. The use of PBSC to increase the stem cell dose is being explored in the EBMT SAAWP protocol for haploidentical HSCT (Clay *et al*, 2014)

??

HLA identical sibling BMT

 # Which patient should be considered for BMT ?


Acquired SAA
HLA = Sib
≤40 yy
Sib BMT

REVIEW

Standard treatment of acquired SAA in adult patients 18–40 years old with an HLA-identical sibling donor

M Aljurf[1], H Al-Zahrani[1], MT Van Lint[2] and JR Passweg[3]

Bone Marrow Transplantation (2013) **48,** 178–179

increasing with time in favor of HSCT over IS. Presently, most centers offer upfront allogeneic transplantation for SAA patients with an available matched sibling donor up to the age of 50 years and selected patients older than 50 who are otherwise in excellent health with disease features suggestive of low likelihood of response to IS therapy, such as very severe AA (ANC below 0.2×10^9/L).

bjh guideline

British Journal of Haematology, 2016, **172**, 187–207

Guidelines for the diagnosis and management of adult aplastic anaemia

Sally B. Killick, Writing Group Chair[1] Nick Bown,[2] Jamie Cavenagh,[3] Inderjeet Dokal,[4] Theodora Foukaneli,[5] Anita Hill,[6] Peter Hillmen,[6] Robin Ireland,[7] Austin Kulasekararaj,[7] Ghulam Mufti,[7] John A. Snowden,[8] Sujith Samarasinghe,[9] Anna Wood, BCSH Task Force Member[10] and Judith C. W. Marsh[7] on behalf of the British Society for Standards in Haematology

- Up-front MSD HSCT for young and adult patients is the treatment of choice for severe AA, but patients aged between 35-50 years need to be carefully assessed for co-morbidities prior to consideration for transplantation. Grade 1B

Fig.2

SAA
HLA id sibs ; 2001-2010

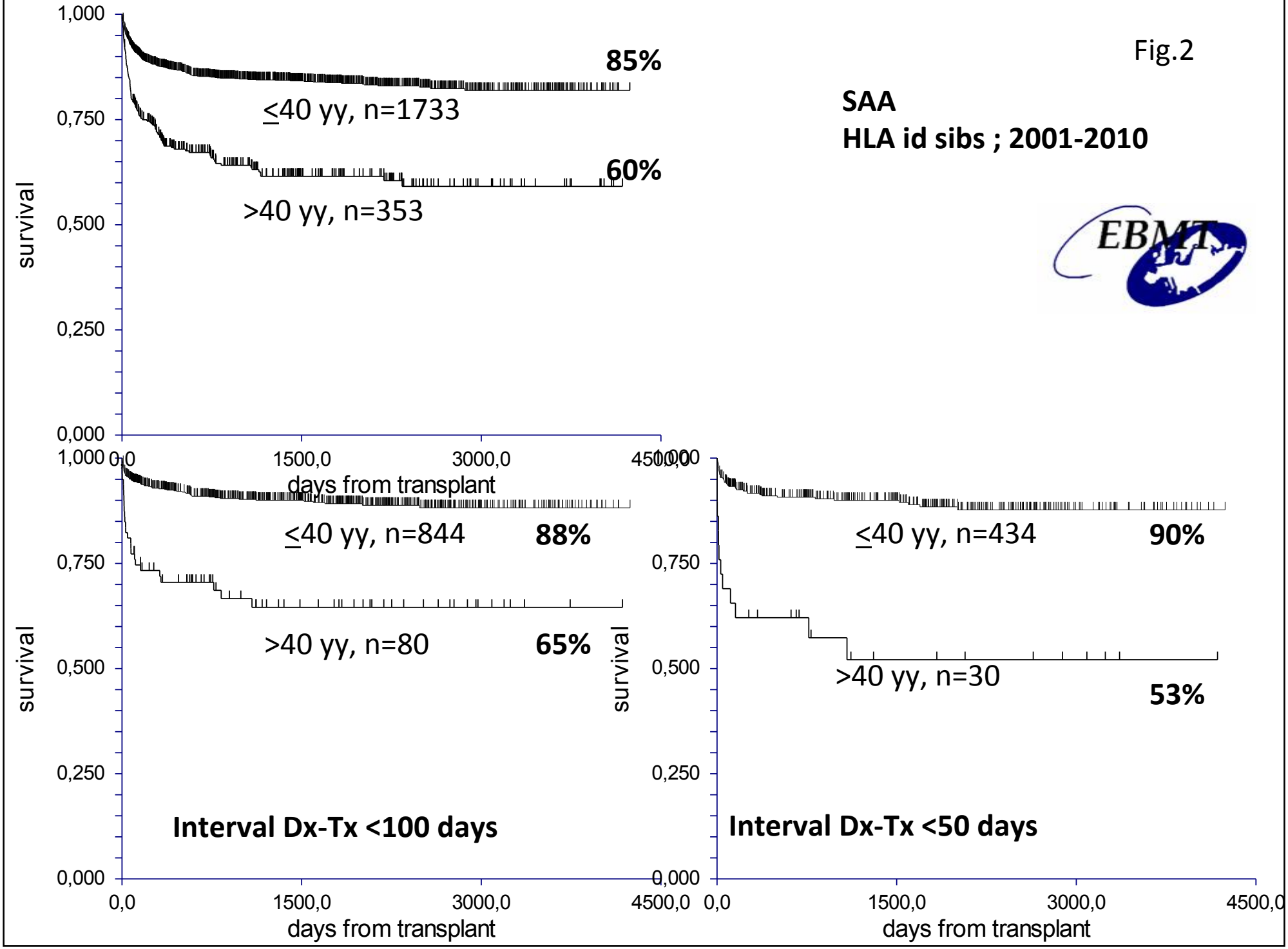
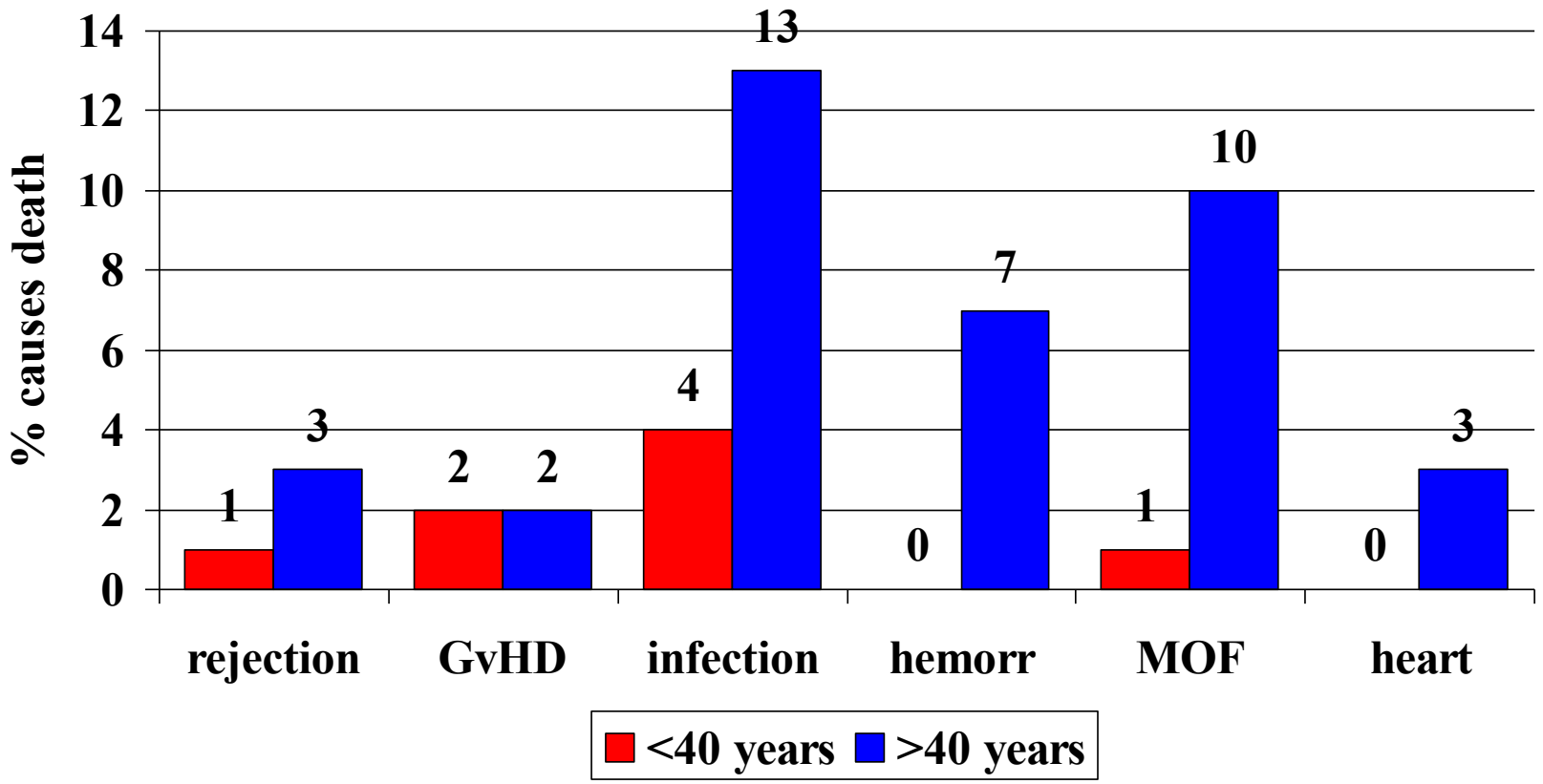


Fig.3

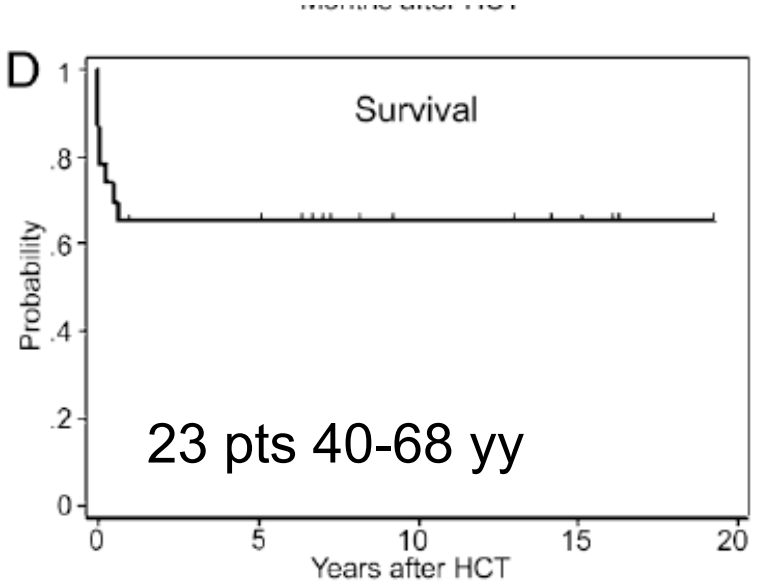
SAA HLA id siblings; 2001-2010
causes of death

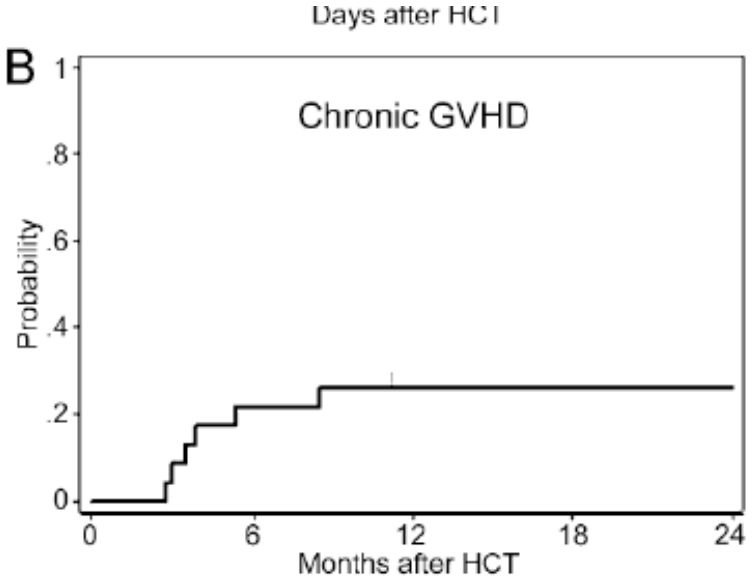


Biol Blood Marrow Transplant. 2010 October ; 16(10): 1411–1418. doi:10.1016/j.bbmt.2010.04.005.

Outcome of Allogeneic Hematopoietic Cell Transplantation from HLA-Identical Siblings for Severe Aplastic Anemia in Patients over 40 Years of Age

Dario Sangiolo[1,*], **Rainer Storb**[1,2], **H. Joachim Deeg**[1,2], **Mary E.D. Flowers**[1,2], **Paul J. Martin**[1,2], **Brenda M. Sandmaier**[1,2], **Hans-Peter Kiem**[1,2], **Richard A. Nash**[1,2], **Kris Doney**[1,2], **Wendy M. Leisenring**[1,3], and **George Earl Georges**[1,2]





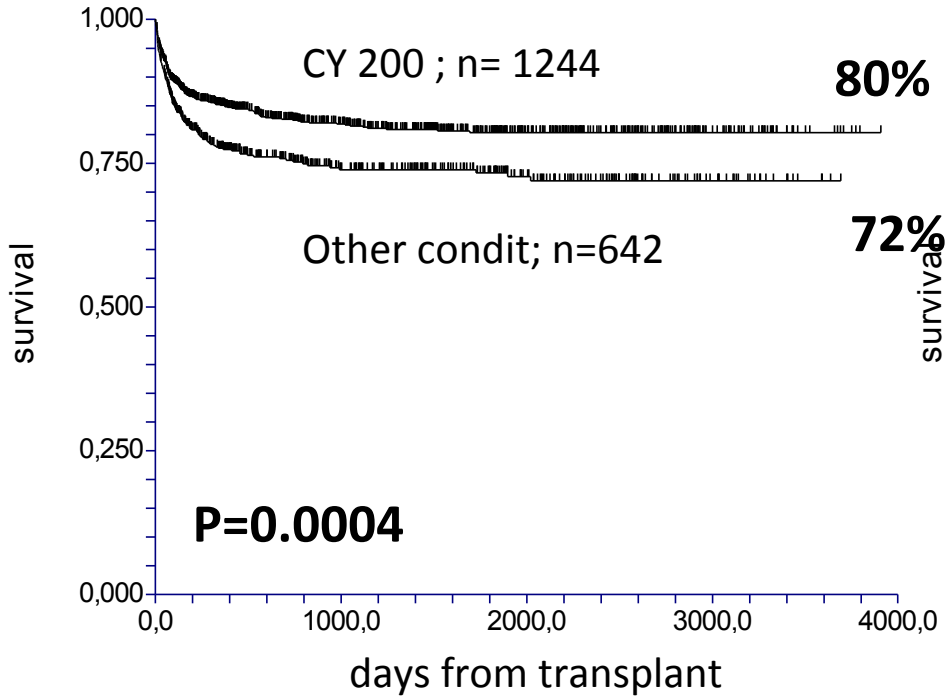
HCT. Our data favor a practice of extending HLA-identical sibling HCT for treatment of SAA in patients older than 40 years of age who are without significant medical comorbidities.

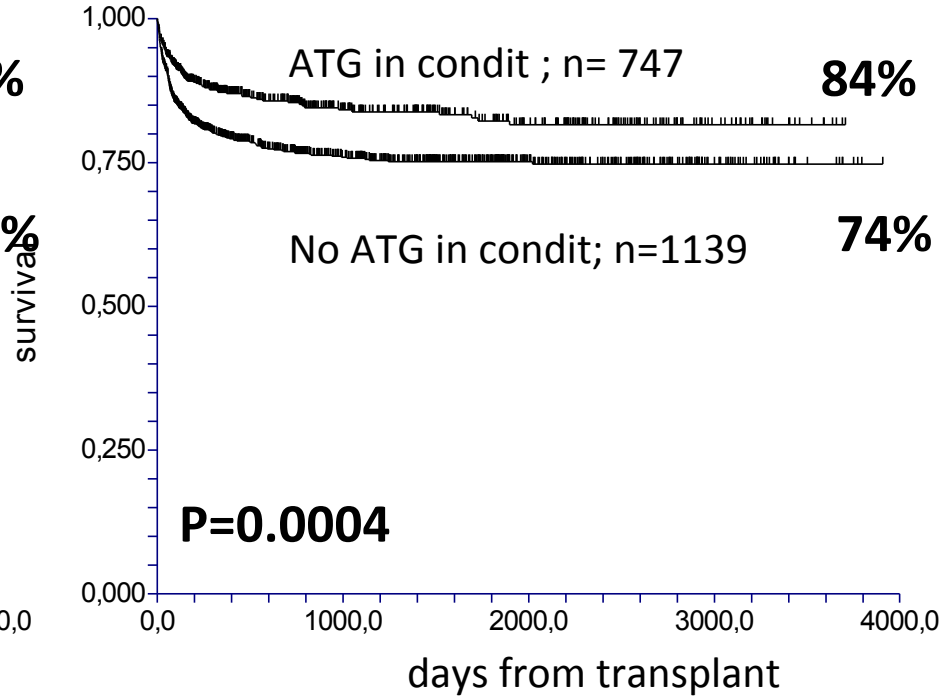
HLA identical sibling BMT

 # Which patient should be considered for BMT ?

 # what conditioning regimen and SC source?

Haematologica. 2012; Aug;97(8):1142-8.





AGE <=20

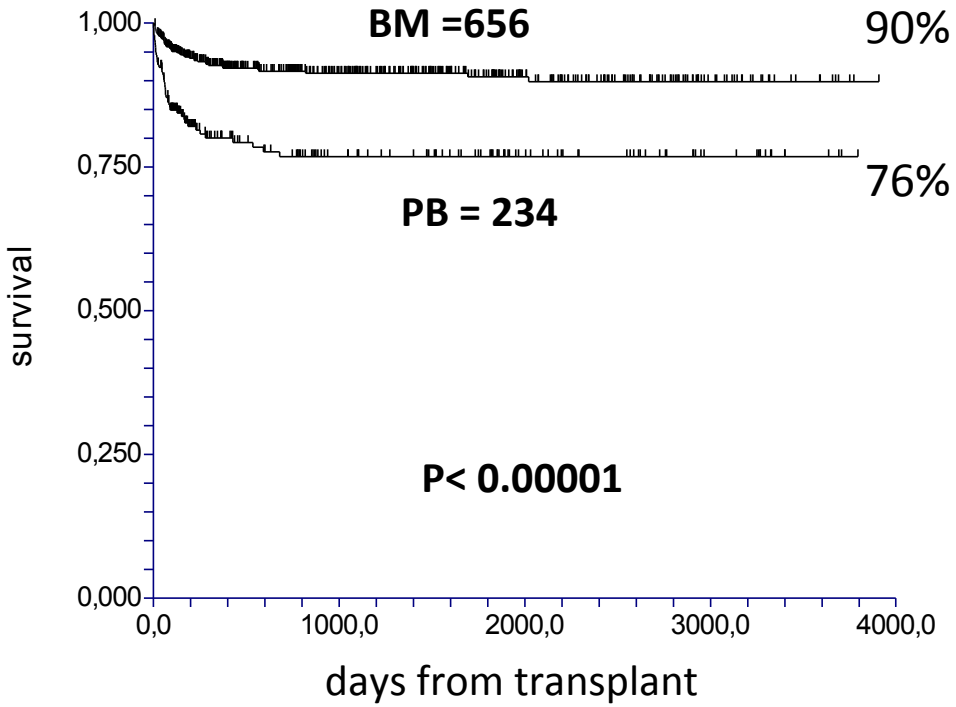


Fig.3a

AGE >20

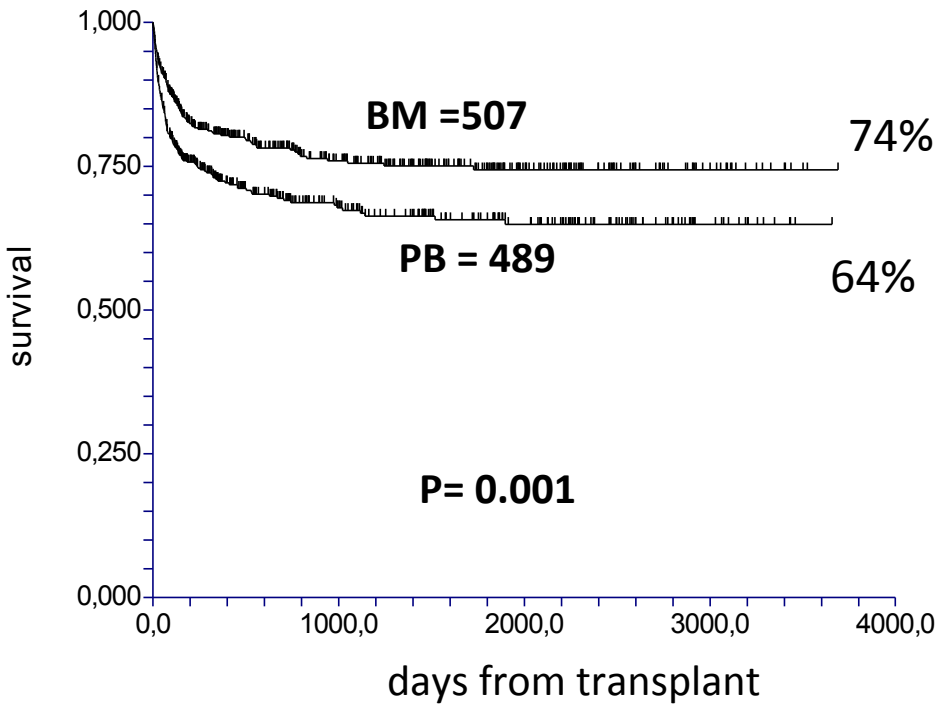


Fig.3b

1. trapianti da fratelli HLA identici

 # prima linea <40 anni

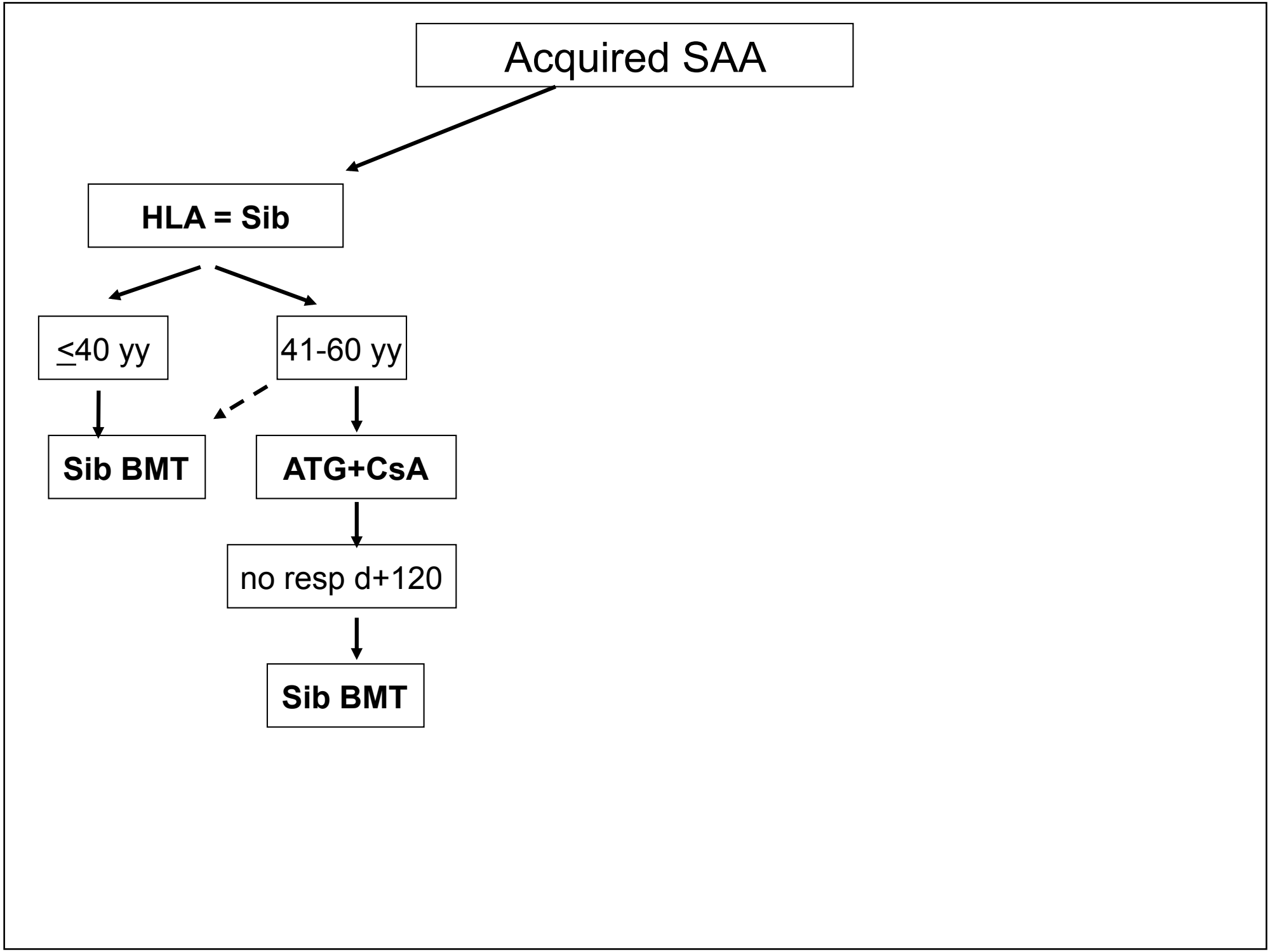
 # condiz CY 200 + ATG + BM (<40)

HLA identical sibling BMT

 # Which patient should be considered for BMT ?

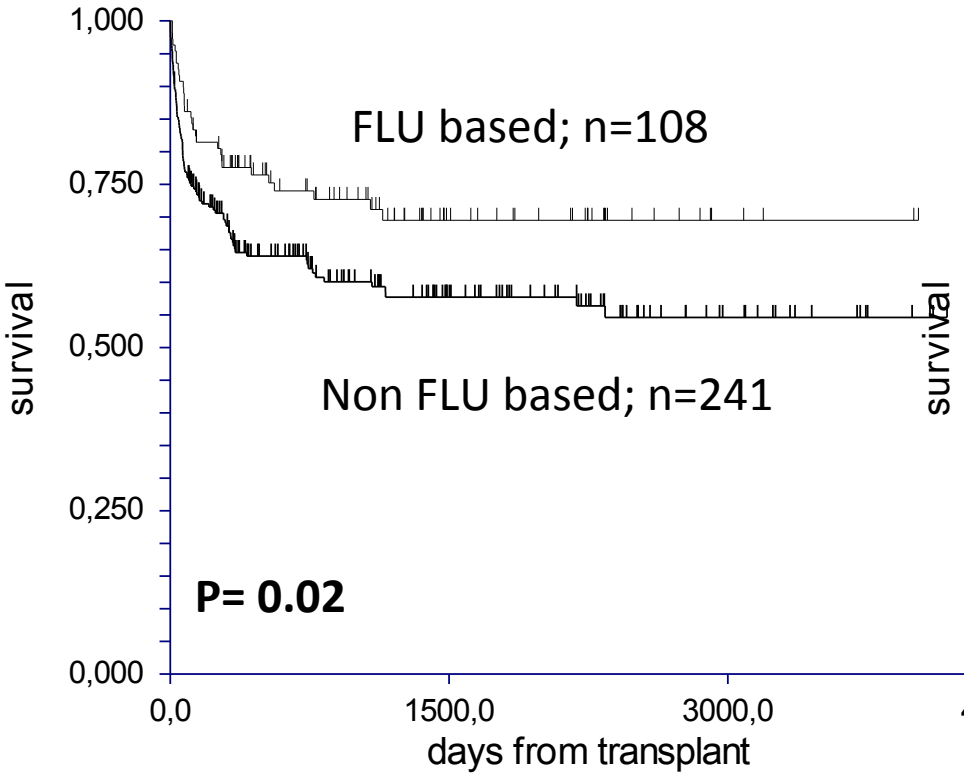
 # what conditioning regimen and SC source?

 # patient over 40 ?


Acquired SAA
HLA = Sib
≤40 yy
41-60 yy
Sib BMT
ATG+CsA
no resp d+120
Sib BMT

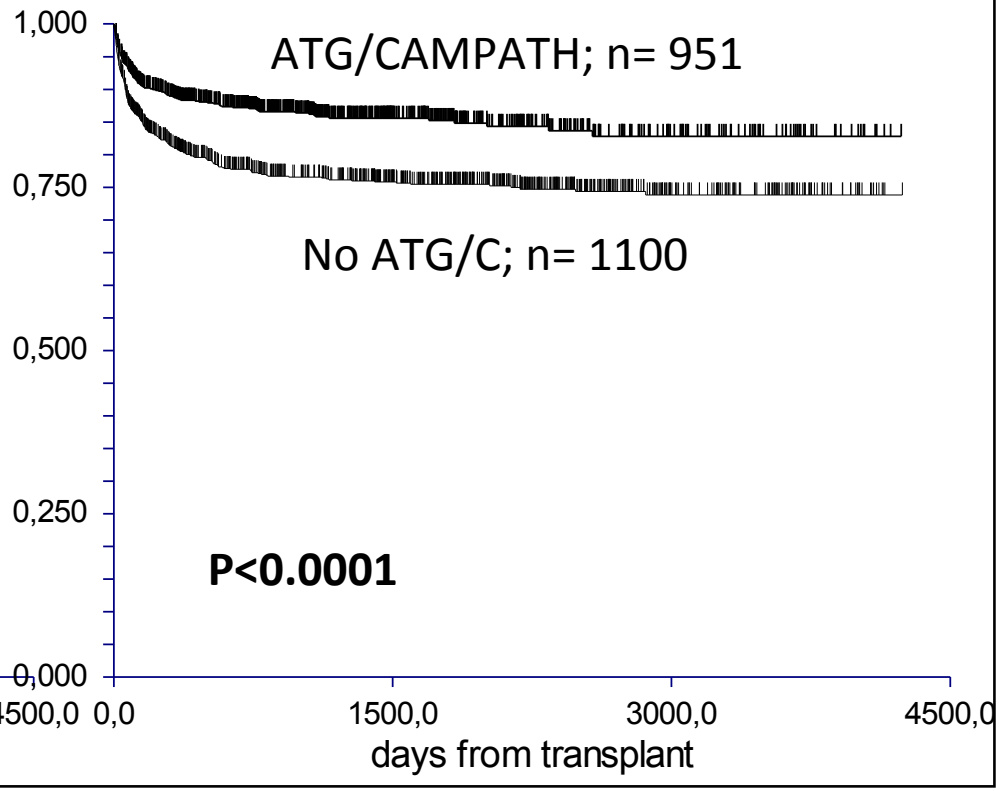
SAA 2001-2010

MSD, Age > 40 years

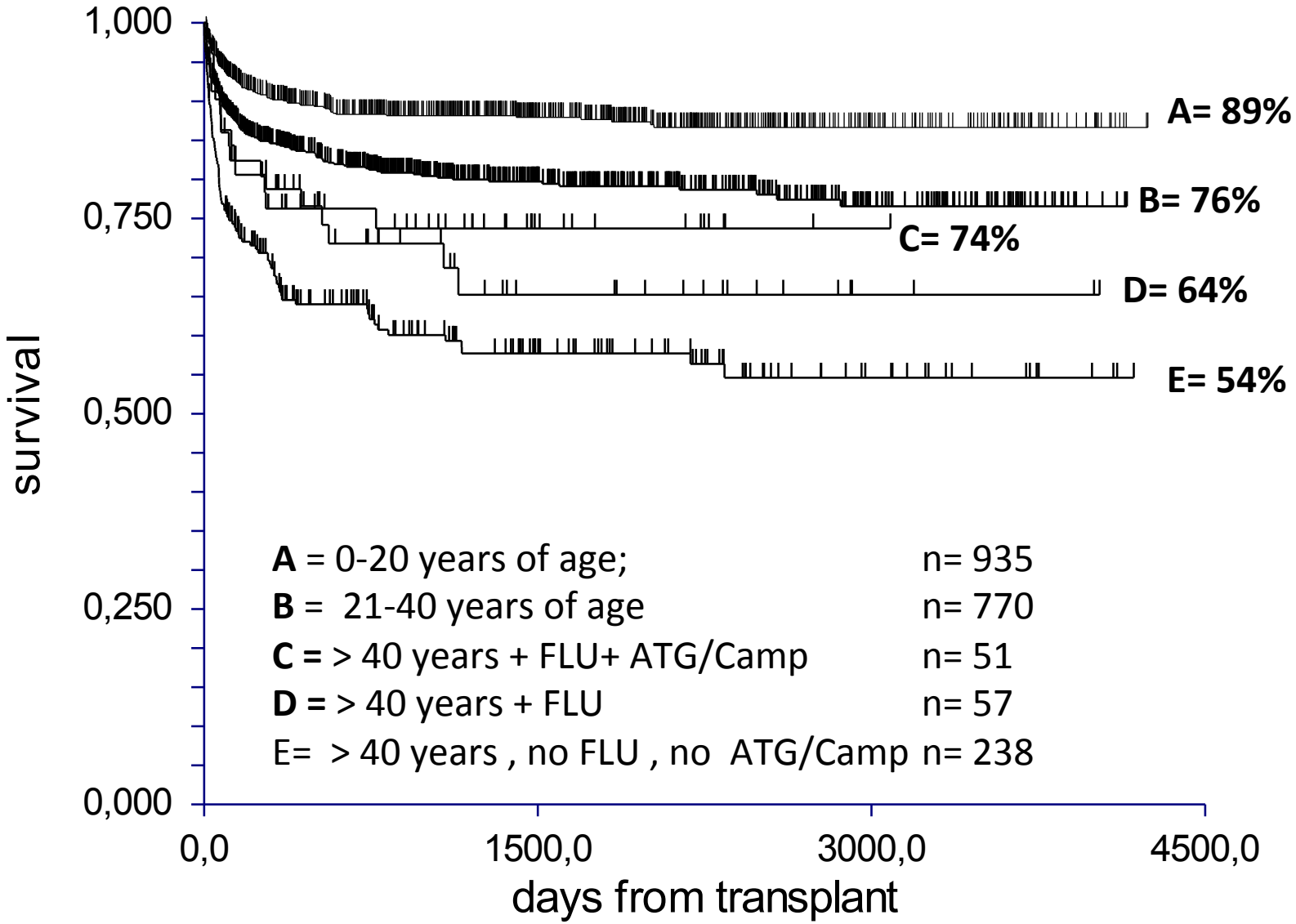


SAA 2001-2010

HLA identical siblings



SAA 2001-2010; HLA id sibling transplants
The effect of age and the role of conditioning regimens



2. trapianti da fratelli HLA identici

prima linea <40 anni

condiz CY 200 + ATG + BM (<40)

seconda linea >40 anni
condiz FLU CY ATG (TBI200?) >40

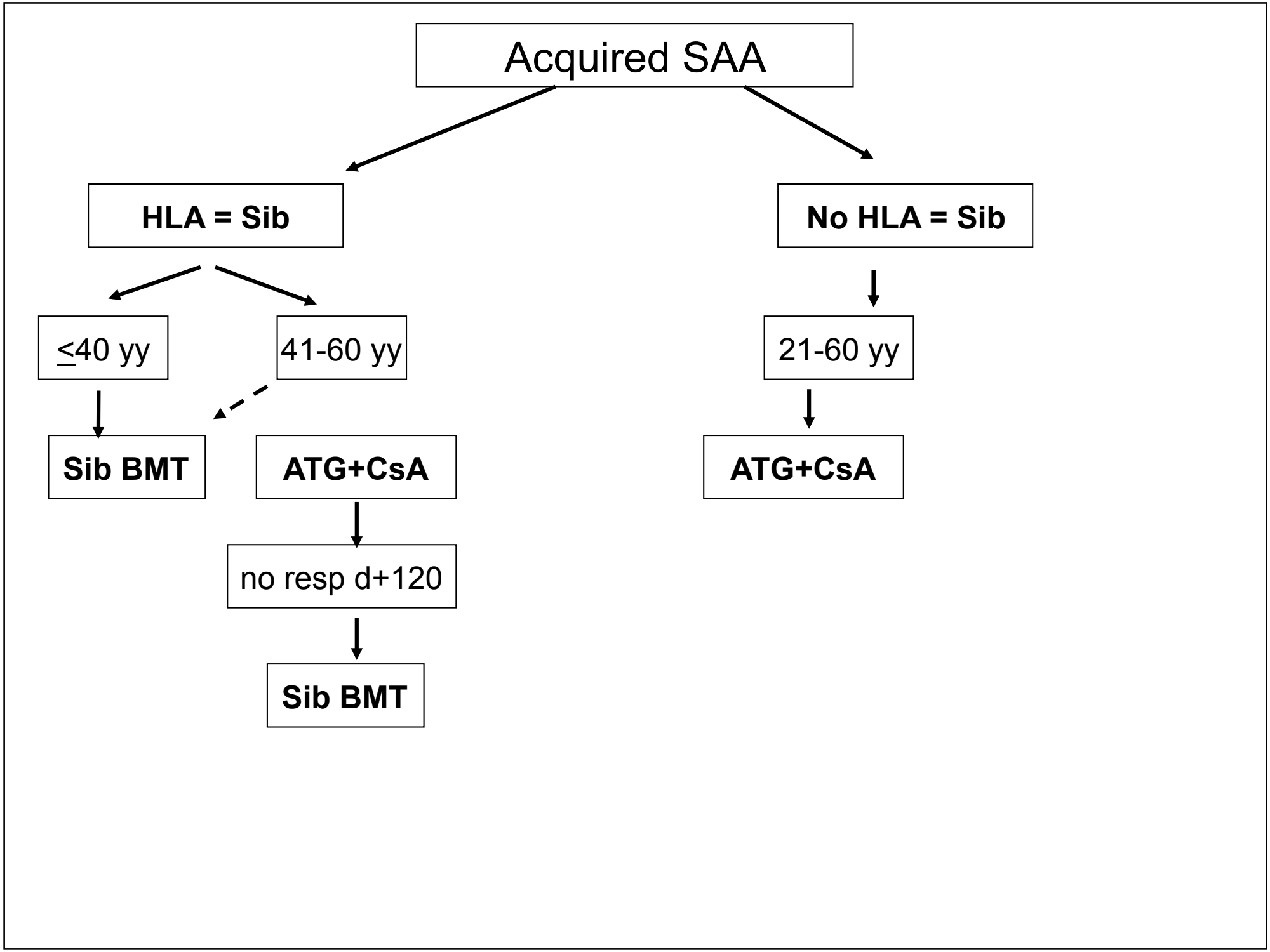
HLA identical sibling BMT

 # Which patient should be considered for BMT ?

 # what conditioning regimen and SC source?

 # patients >40 year

 # patients without a matched SIB ?

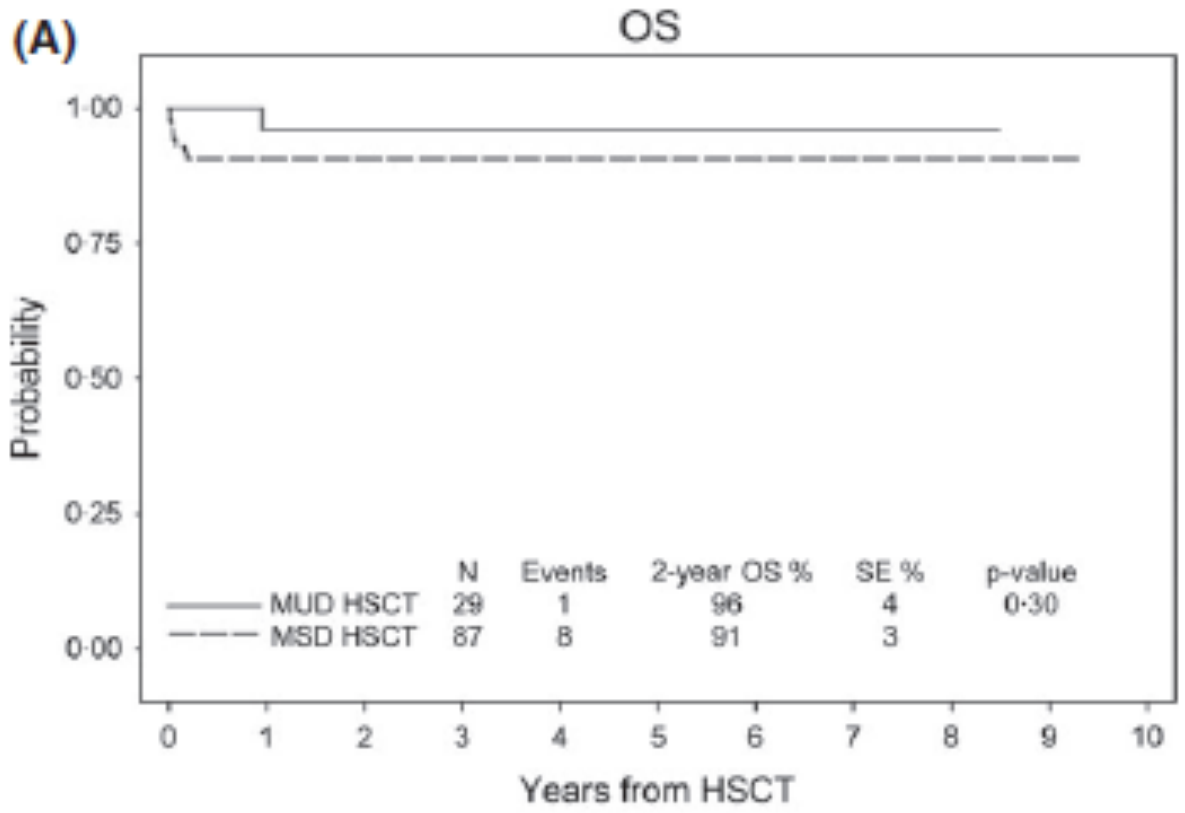

Acquired SAA
HLA = Sib
No HLA = Sib
≤40 yy
41-60 yy
21-60 yy
Sib BMT
ATG+CsA
ATG+CsA
no resp d+120
Sib BMT

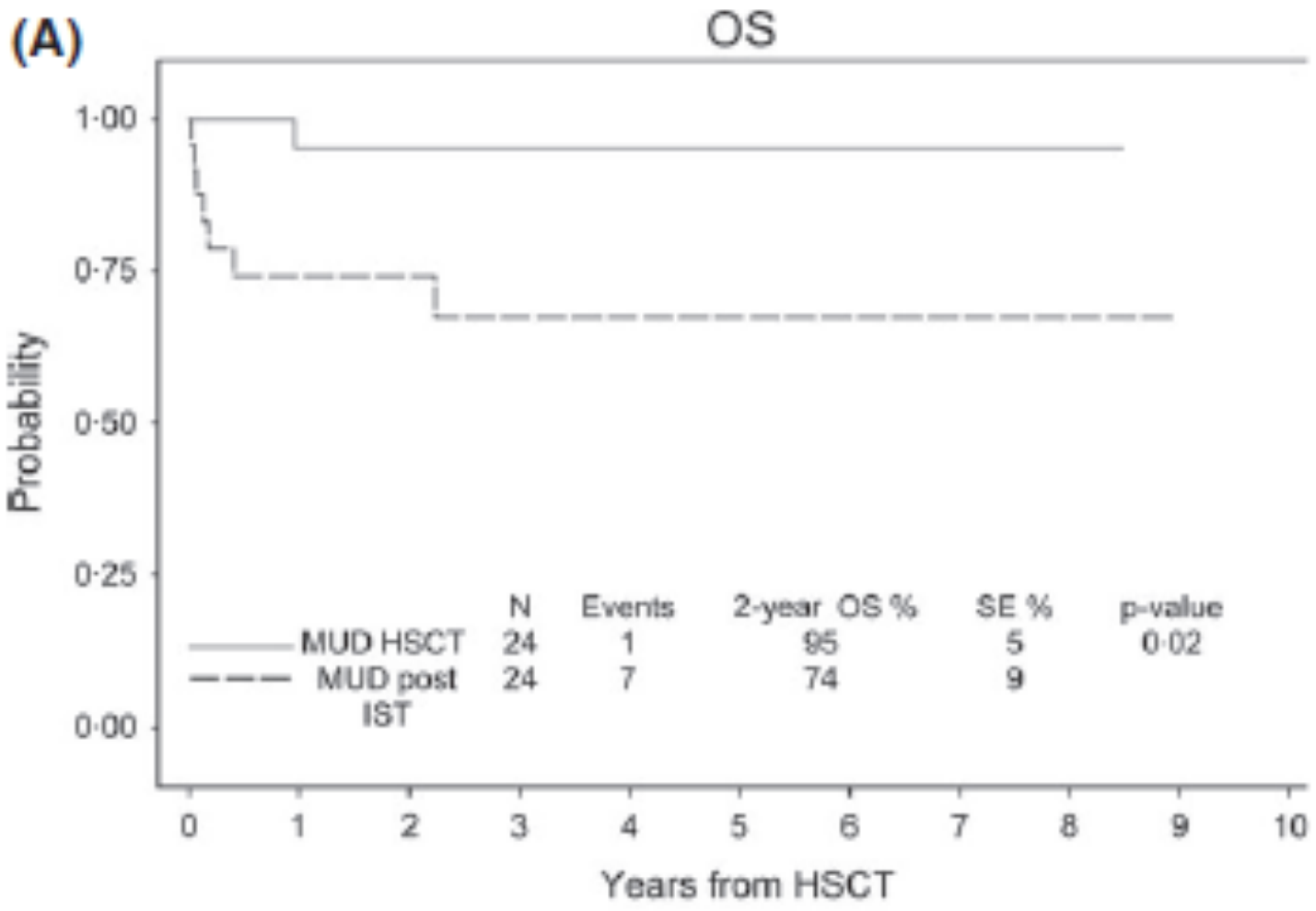
bjh research paper British Journal of Haematology, 2015, 171, 585–594

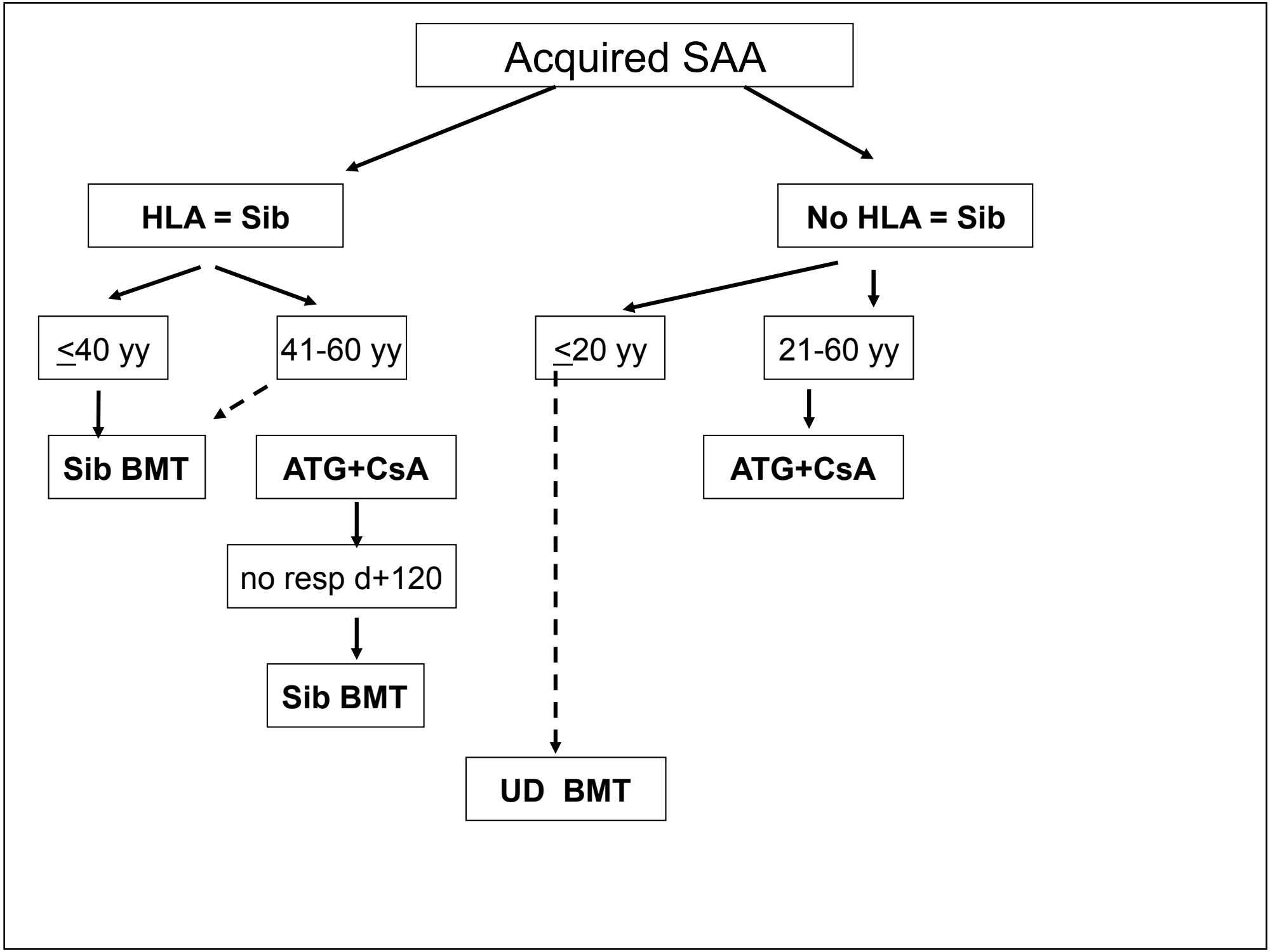
Similar outcome of upfront-unrelated and matched sibling stem cell transplantation in idiopathic paediatric aplastic anaemia. A study on behalf of the UK Paediatric BMT Working Party, Paediatric Diseases Working Party and Severe Aplastic Anaemia Working Party of EBMT

N=29

Age 0.5-18




(A)
OS
1·00
0·75
0·50
0·25
0·00
Probability
N
Events
2-year OS %
SE %
p-value
MUD HSCT
24
1
95
5
0·02
MUD post IST
24
7
74
9
0
1
2
3
4
5
6
7
8
9
10
Years from HSCT


Acquired SAA
HLA = Sib
No HLA = Sib
≤40 yy
41-60 yy
≤20 yy
21-60 yy
Sib BMT
ATG+CsA
ATG+CsA
no resp d+120
Sib BMT
UD BMT

HLA identical sibling BMT

 # Which patient should be considered for BMT ?
 # what conditioning regimen and SC source?
 # patients >40 year
 # patients without a matched SIB ?
 # second line Unrelated BMT ?

Unrelated donor transplants for SAA; (EBMT 2005-2009)

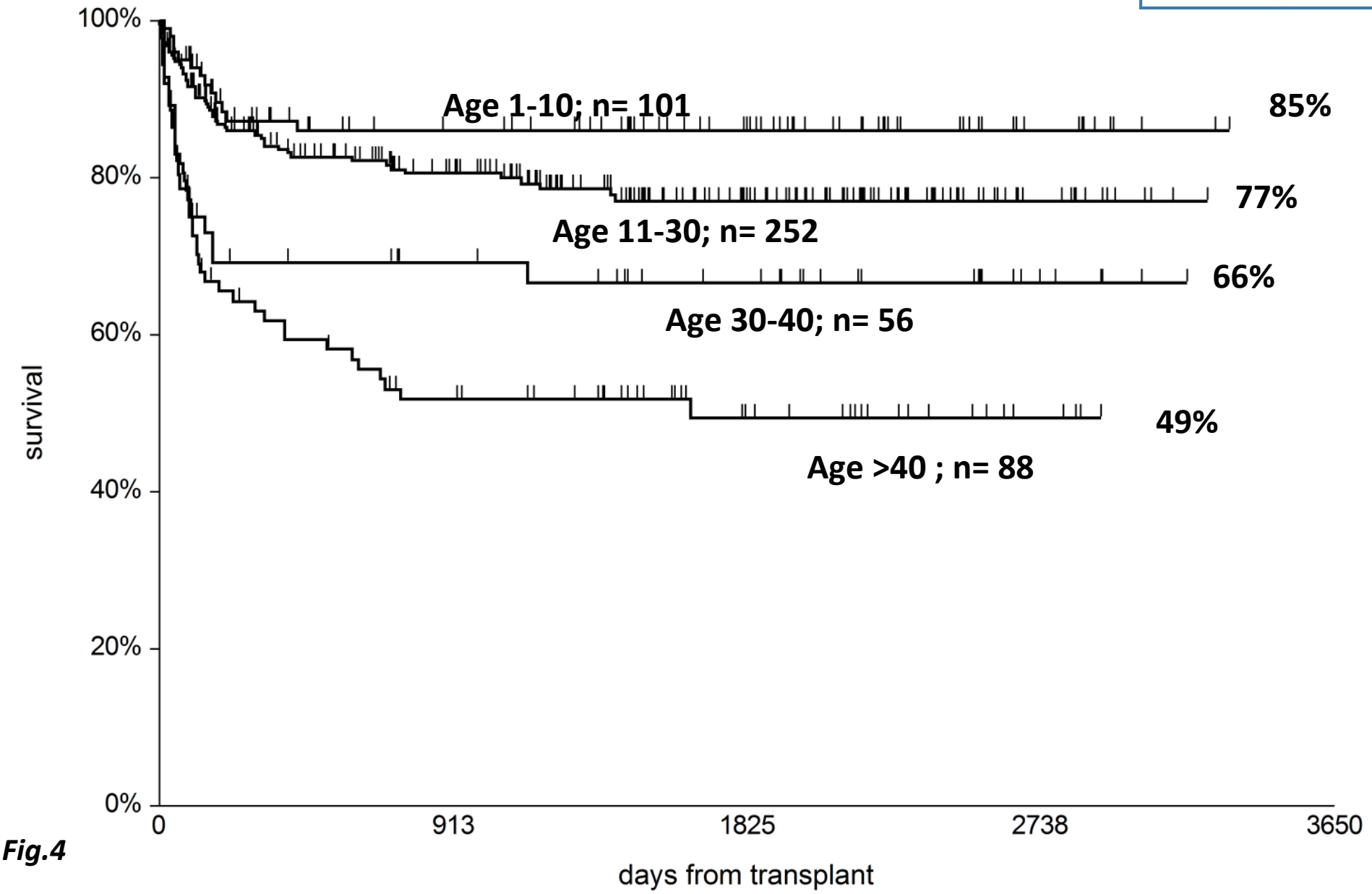


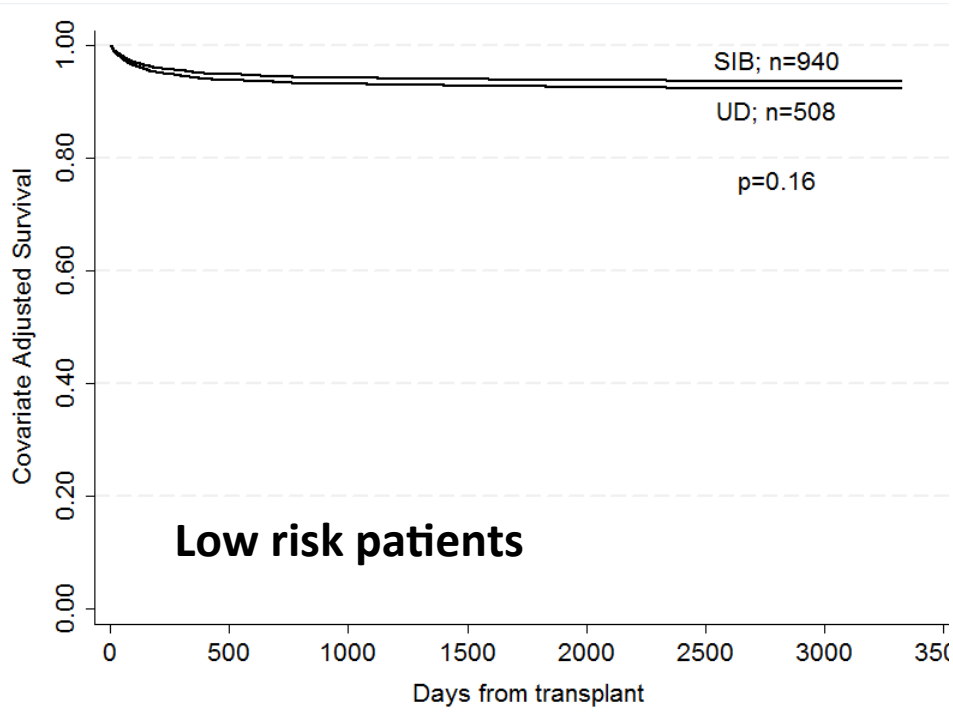
Fig.4

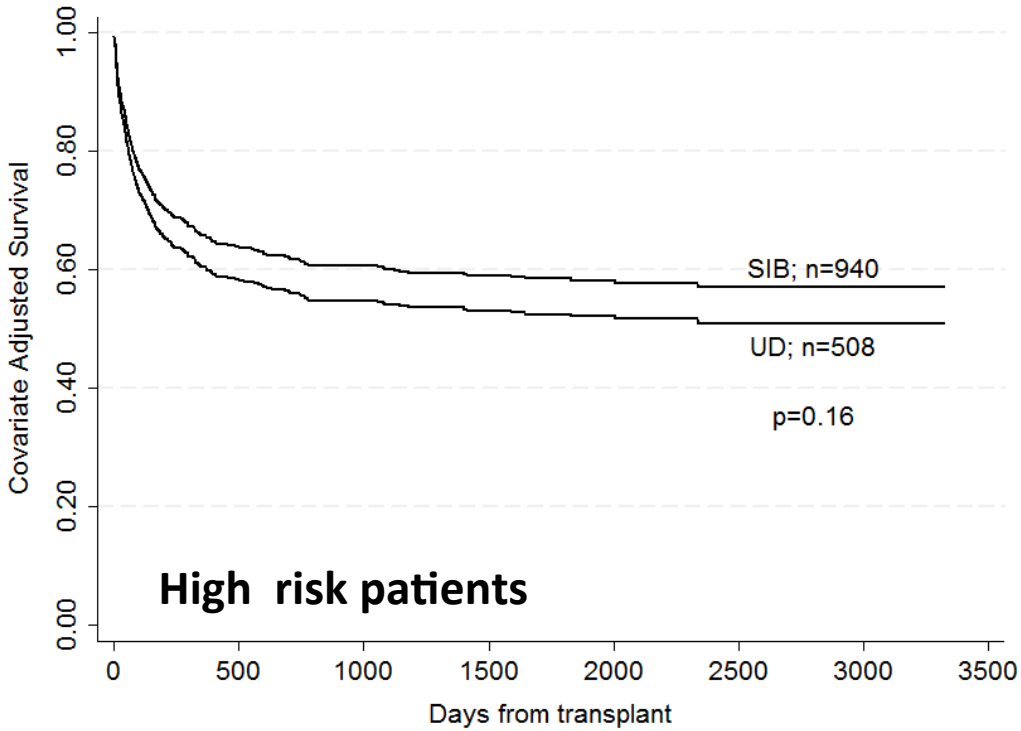
ALLOGENEIC TRANSPLANTS FOR APLASTIC ANEMIA

Haematologica 2015; 100; 696

EBMT analysis 2014: **1448 patients**

Adjusted effect of donor type (UD vs SIB) derived from the multivariate analysis
After adjusting for AGE, interval DxTx, use of ATG, use of BM/PB, and CMV status)





Low risk= age<20; ATG; BM; DxTx <180 dd
CMV D-/R-

High risk: Age ≥20; no ATG; PB; DxTx ≥180
CMV other than D-/R-

Fig. 1a Acute II-IV GvHD

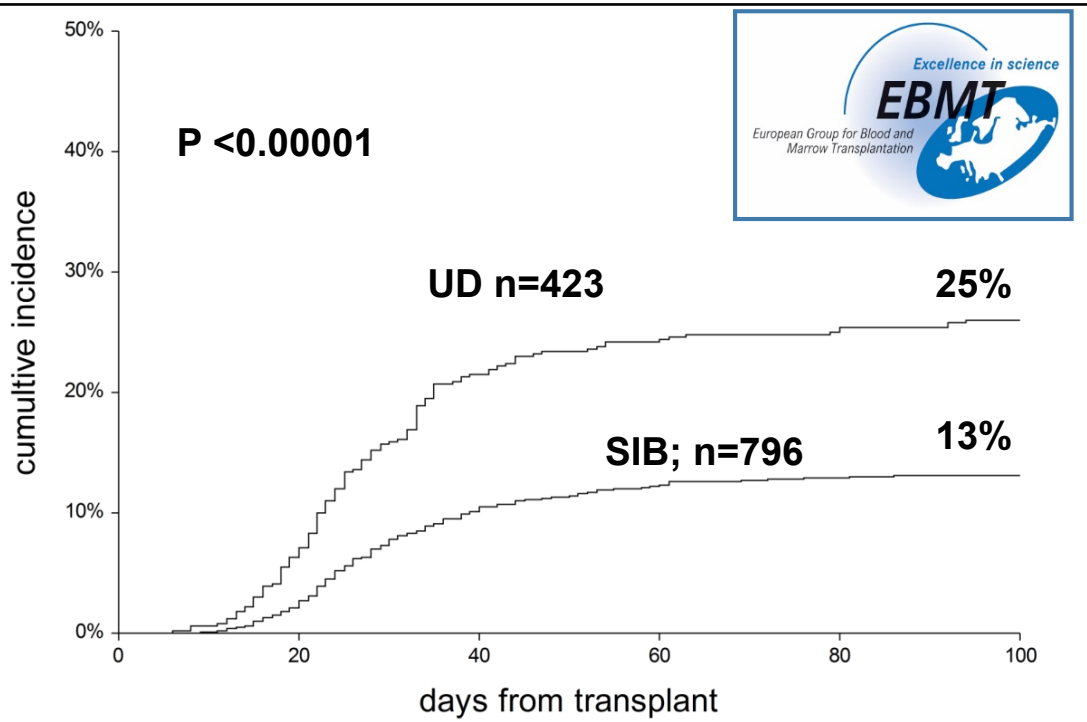
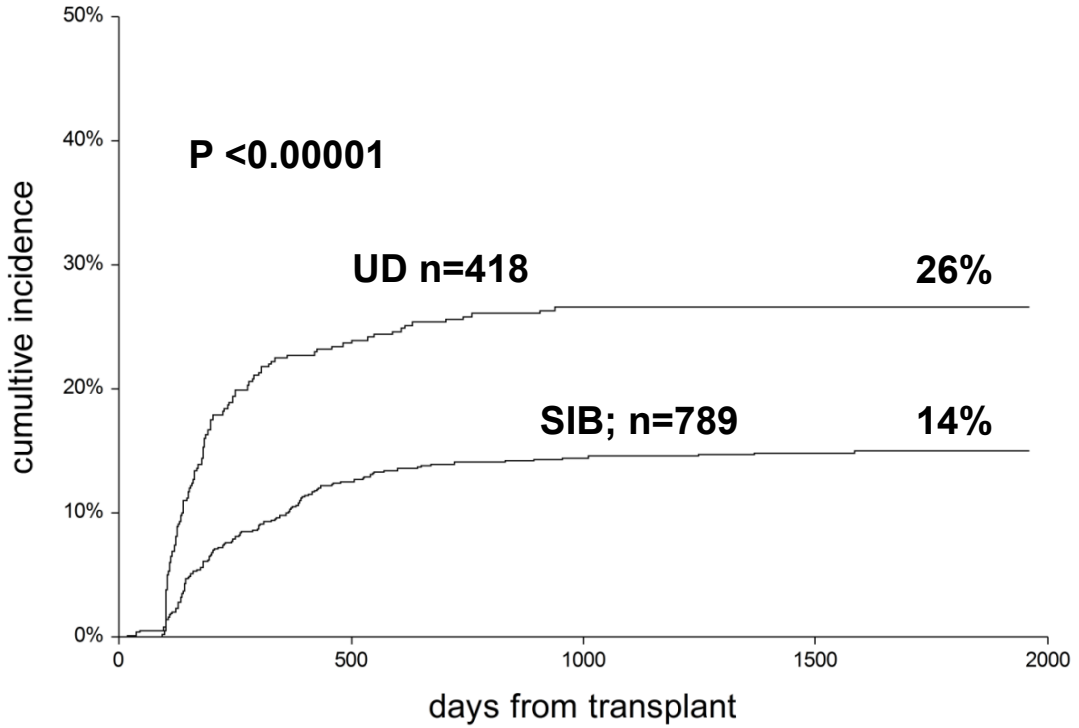


Fig. 1b Chronic GvHD



HLA identical sibling BMT

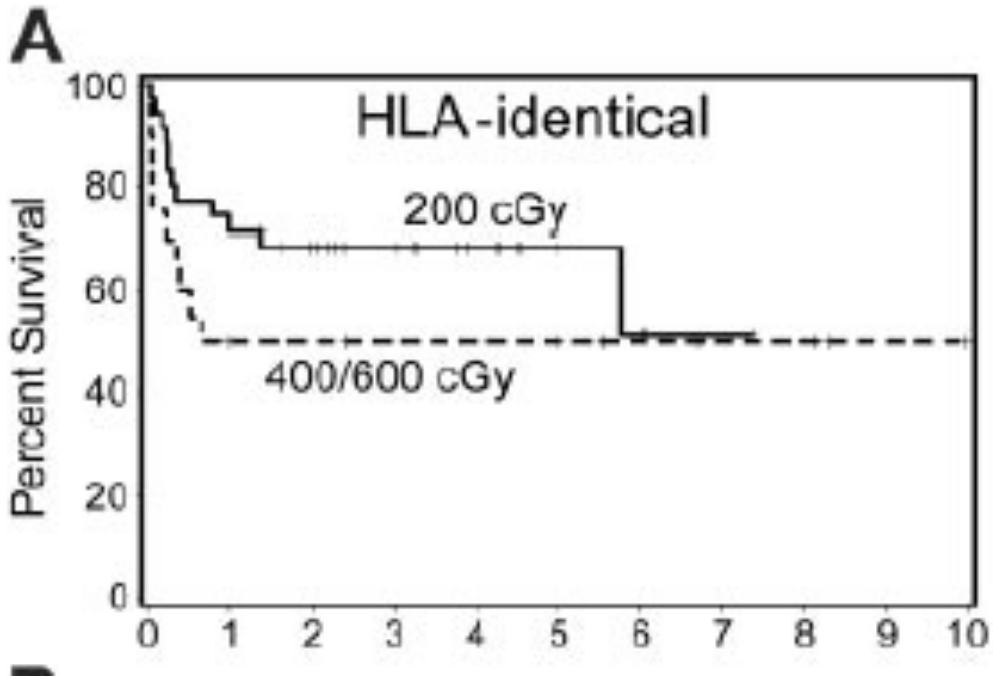
 # Which patient should be considered for BMT ?
 # what conditioning regimen and SC source?
 # patients >40 year
 # patients without a matched SIB ?
 # second line Unrelated BMT ?
 # FC-TBI: TBI dose , CY dose

blood

2006 108: 1485-1491
Prepublished online May 9, 2006;
doi:10.1182/blood-2006-03-005041

Optimization of conditioning for marrow transplantation from unrelated donors for patients with aplastic anemia after failure of immunosuppressive therapy

H. Joachim Deeg, Margaret O'Donnell, Jakub Tolar, Rajni Agarwal, Richard E. Harris, Stephen A. Feig, Mary C. Territo, Robert H. Collins, Peter A. McSweeney, Edward A. Copelan, Shakila P. Khan, Ann Woolfrey and Barry Storer



Cyclophosphamide conditioning in patients with severe aplastic anaemia given unrelated marrow transplantation: a phase 1–2 dose de-escalation study

Paolo Anderlini, Juan Wu, Iris Gersten, Marian Ewell, Jakob Tolar, Joseph H Antin, Roberta Adams, Sally Arai, Gretchen Eames, Mitchell E Horwitz, John McCarty, Ryotaro Nakamura, Michael A Pulsipher, Scott Rowley, Eric Leifer, Shelly L Carter, Nancy L DiFronzo, Mary M Horowitz, Dennis Confer, H Joachim Deeg, Mary Eapen**

Lancet Haematol 2015; 2: e367–75

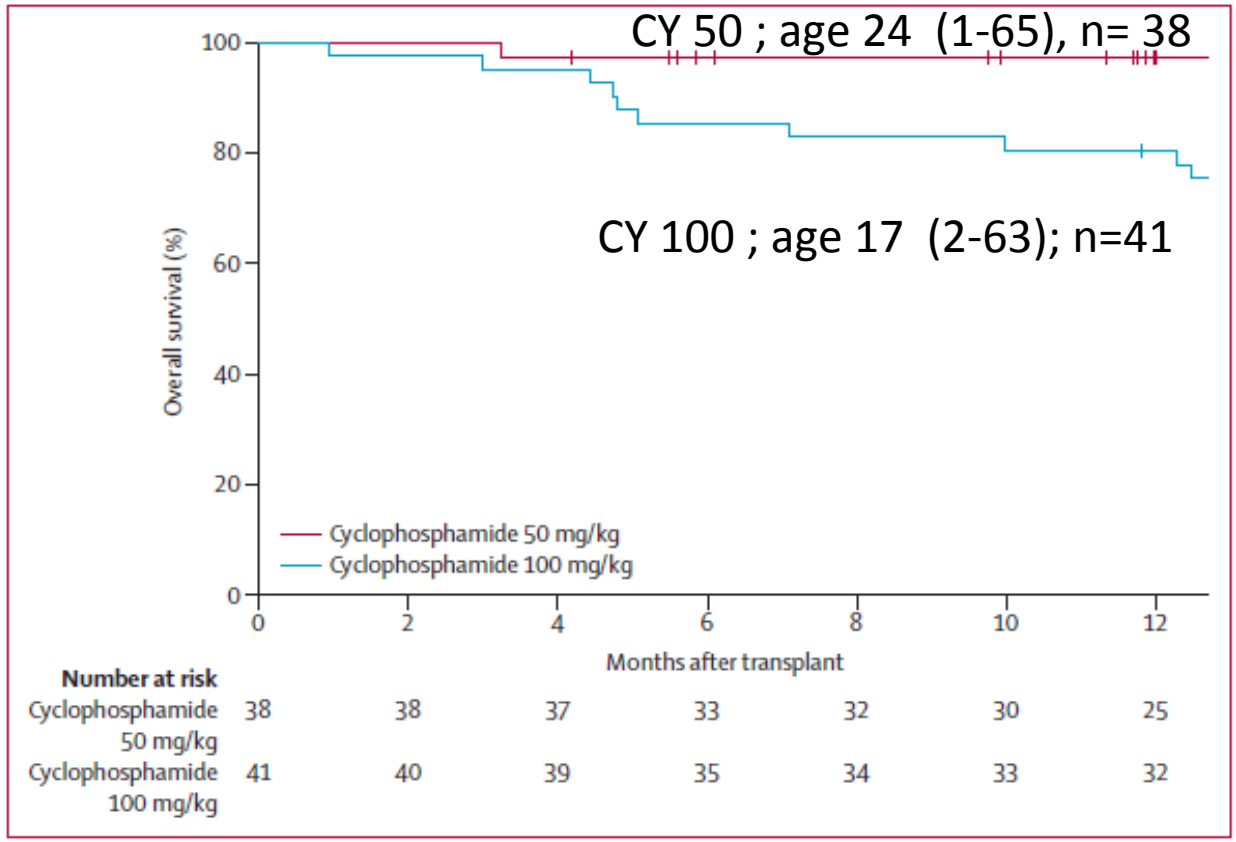


Figure 2: **Overall survival by cyclophosphamide dose**

CY 50 vs 100 mg /kg
FLU 30 mg/m^2 x4
TBI 200

blood
2011 118: 2618-2621
doi:10.1182/blood-2011-05-354001 originally published online June 15, 2011

Effect of stem cell source on outcomes after unrelated donor transplantation in severe aplastic anemia

Mary Eapen, Jennifer Le Rademacher, Joseph H. Antin, Richard E. Champlin, Jeanette Carreras, Joseph Fay, Jakob R. Passweg, Jakub Tolar, Mary M. Horowitz, Judith C. W. Marsh and H. Joachim Deeg

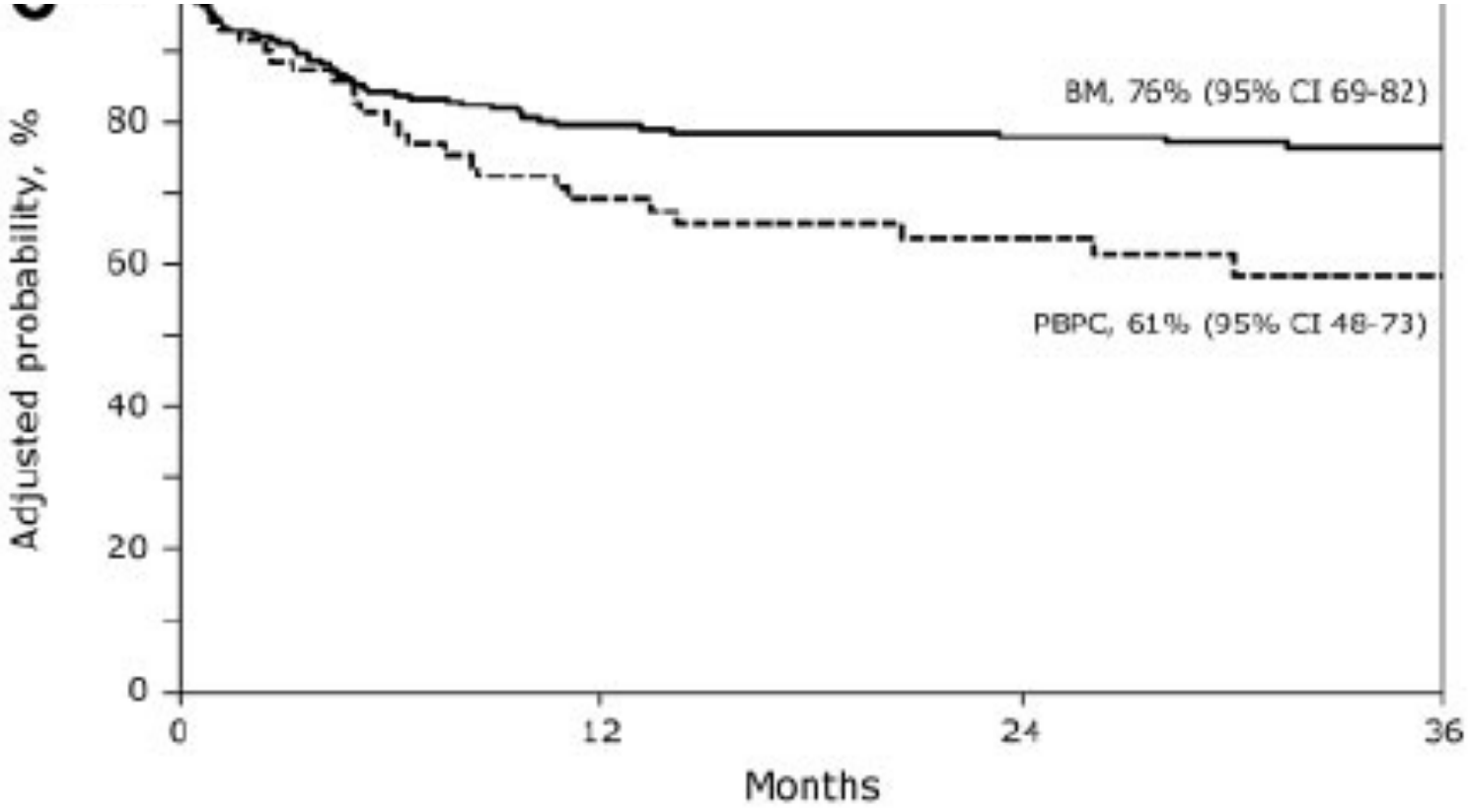
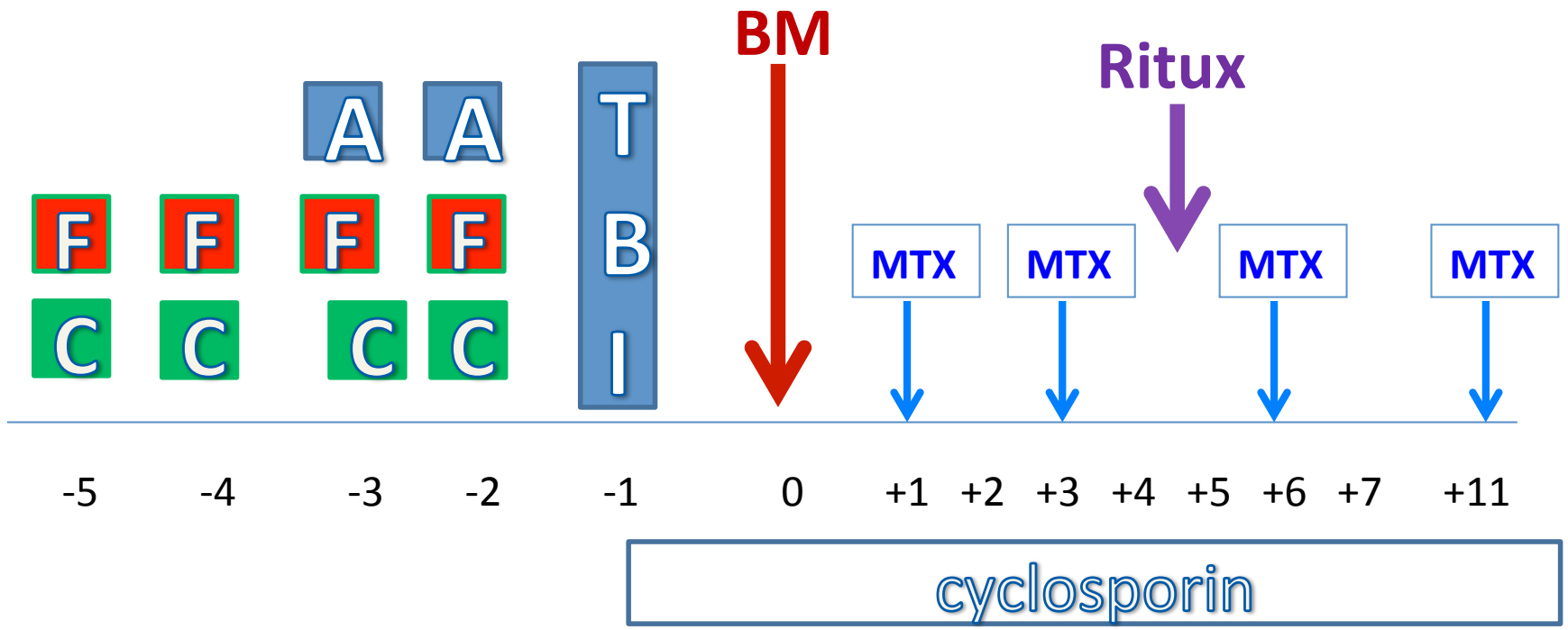


Fig.1 = conditioning regimen for UD transplants in acquired SAA



F — FLUDARABINE 30 mg/m^2/day x4

C — CYCLOPHOSPHAMIDE 30 mg/kg/day x4

A — ATG : dosing depends on ATG brand; see text

TBI — Total body irradiation 2 Gy

Conditioning regimens and survival in SAA (n=58) San Martino Genova 2001-2015

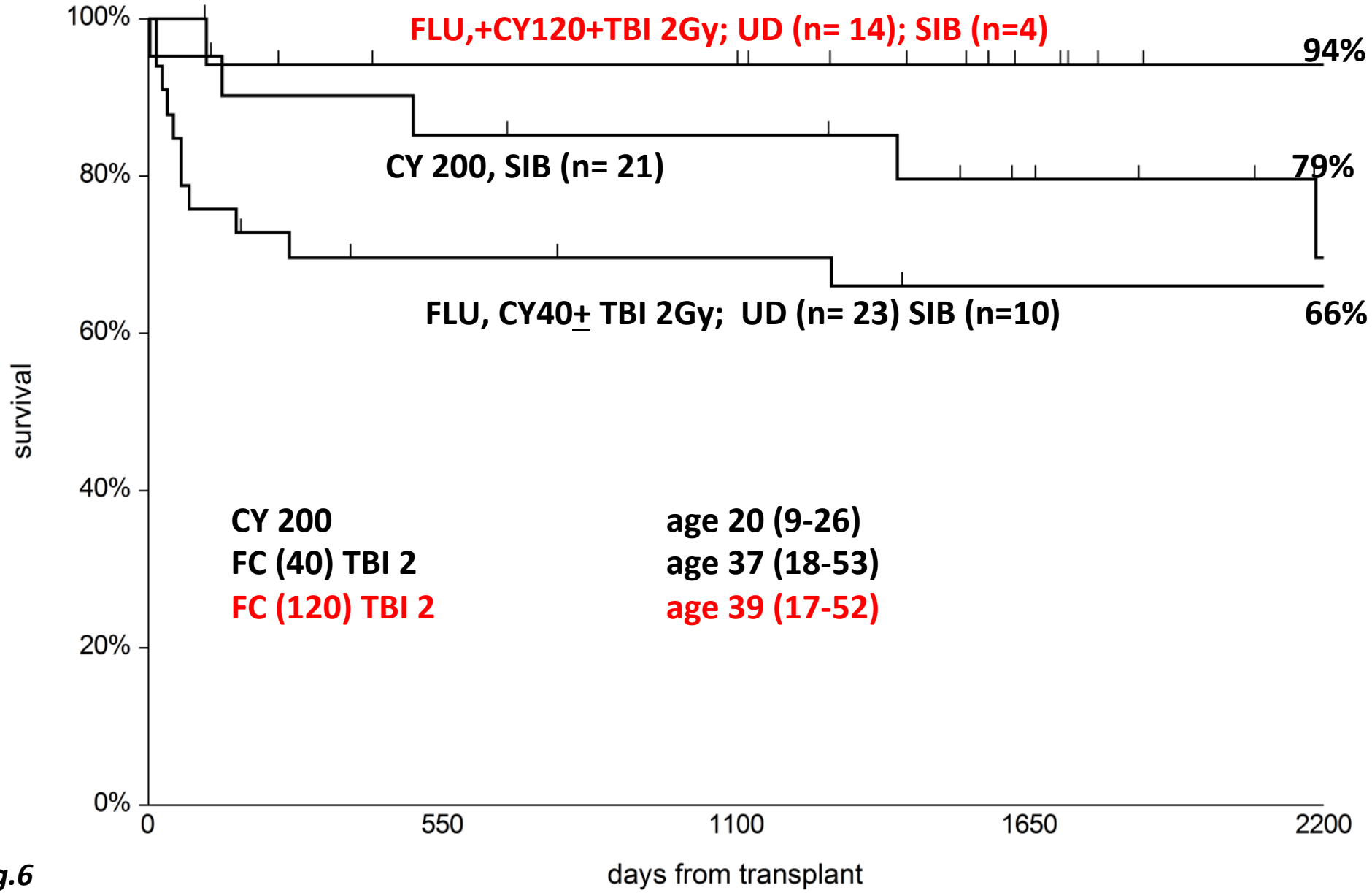
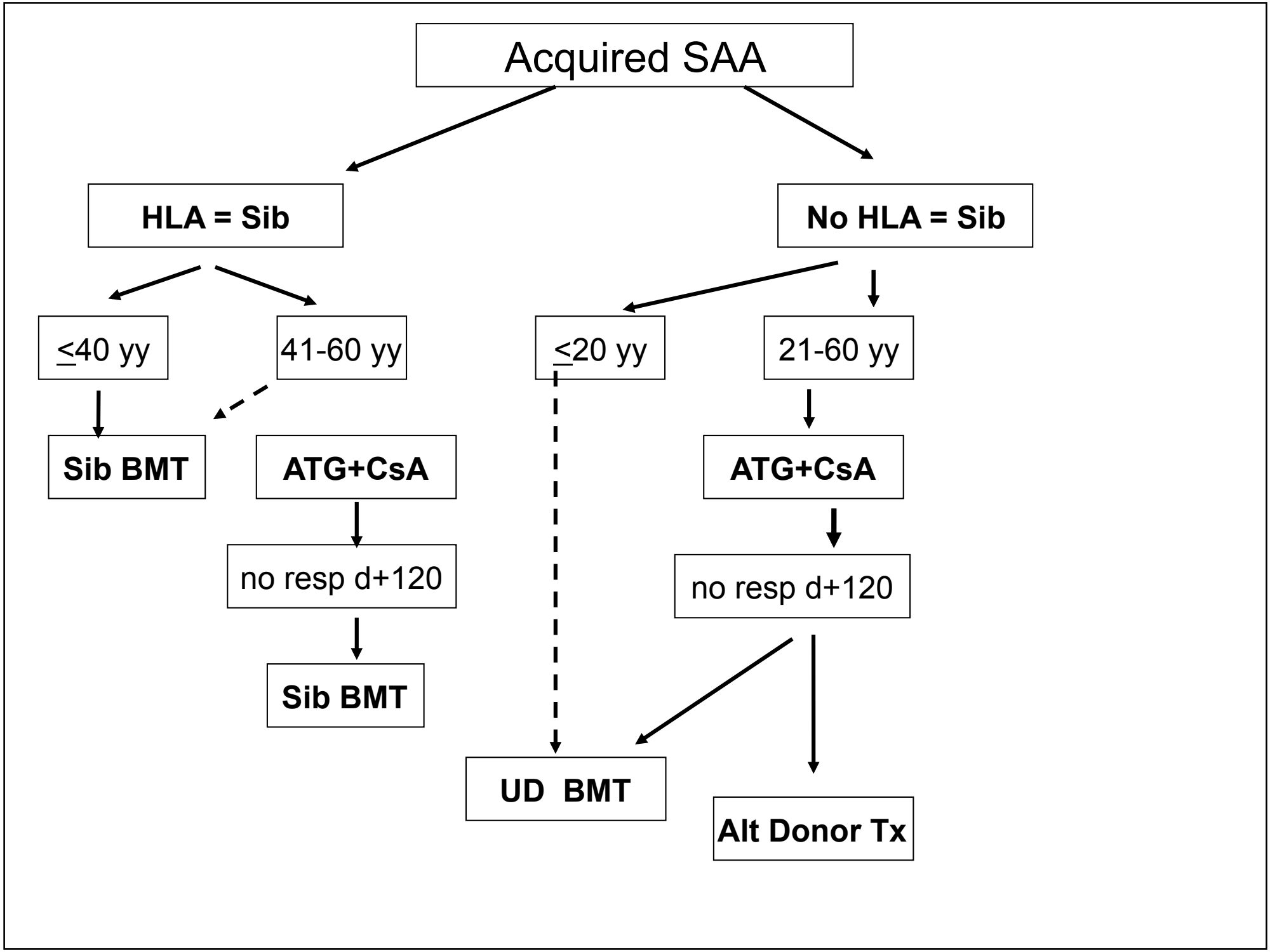


Fig.6


Acquired SAA
HLA = Sib
No HLA = Sib
≤40 yy
41-60 yy
≤20 yy
21-60 yy
Sib BMT
ATG+CsA
ATG+CsA
no resp d+120
no resp d+120
Sib BMT
UD BMT
Alt Donor Tx

3. trapianti da donatori UD

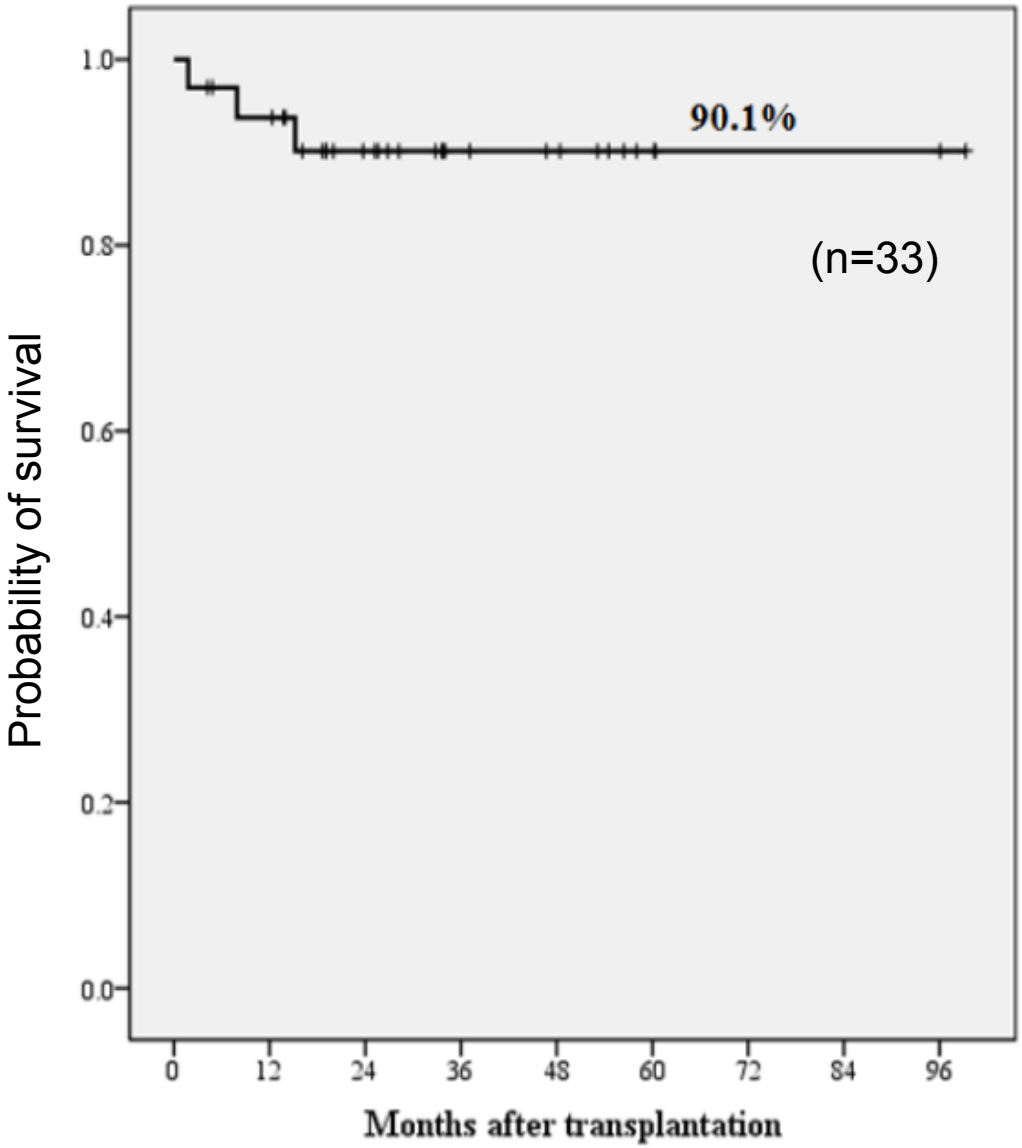
seconda linea (? < 20 anni?)

condizionamento
FLU CY ATG TBI 200

sorgente BM

GvHD prof ATG Cya MTX

Haploidentical HSCT for Childhood SAA

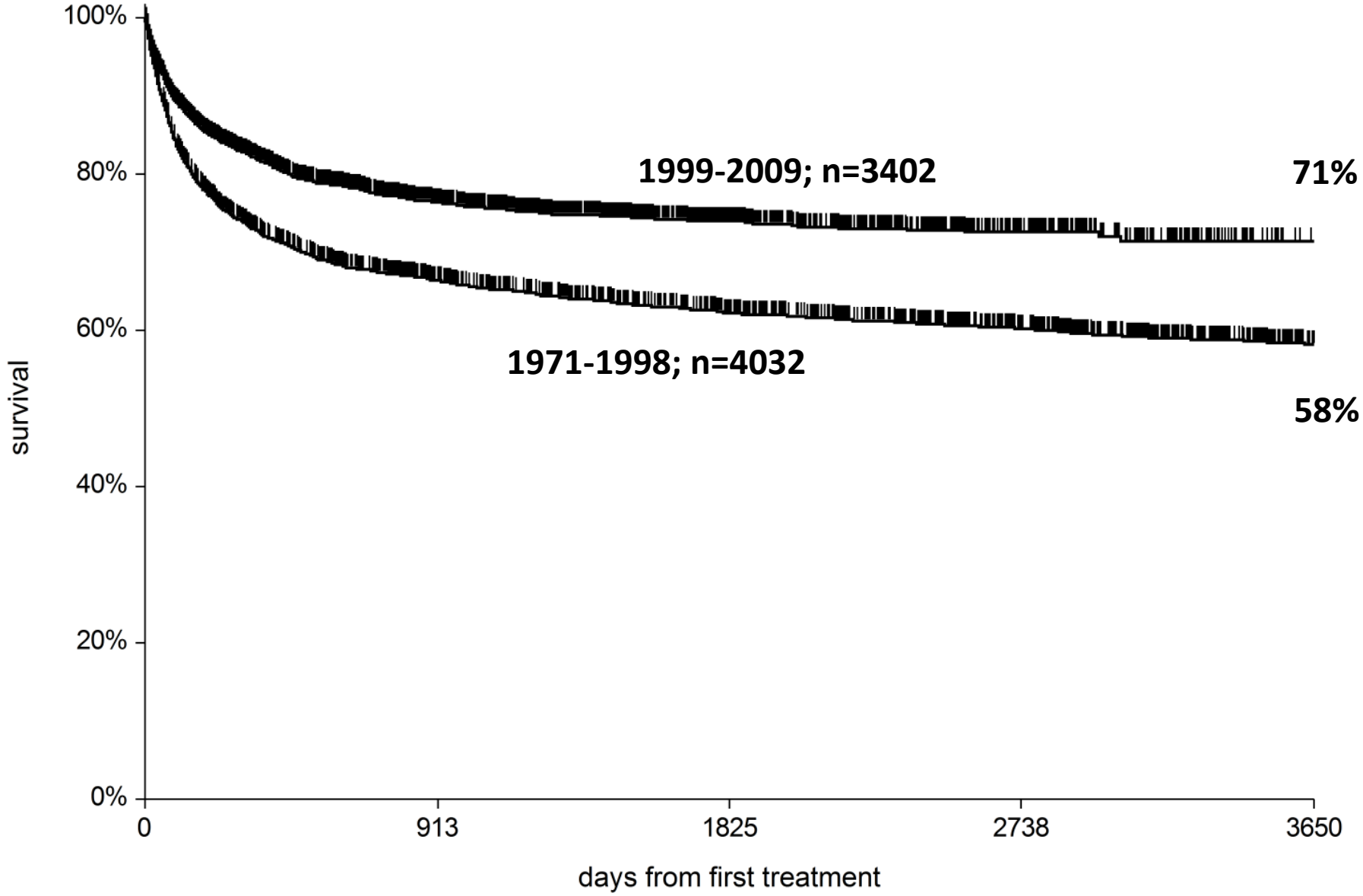


Nagoya, Shanghai, Asan(Seoul)

Conditioning regimen	Primary GF, n (%)	GVHD, n (%)		Survival
		Acute≥II	Chronic	
BU, CY, ATG	0 (0)	8 (42)	9 (56)	65% at 2 yr
FLU, CY, ATG±TBI	1 (8.3)	3 (33)	2 (22)	100% at 1 yr
FLU, CY, ATG	1 (3.8)	3 (12)	10 (40)	85% at 3 yr
BU, FLU, CY, ATG	0 (0)	5 (29)	4 (27)	72% at 1 yr
FLU, CY, TBI	2 (25)	1 (13)	0 (0)	75% at 1 yr
FLU, CY, TBI	1 (6)	2 (13)	3 (20)	67% at 1 yr
FLU, CY, ATG±TBI	1 (4.8)	6 (30)	2 (10)	94% at 3 yr

Total 119 patients
Average OS 79%

Survival of patients with acquired SAA (N=7434) , receiving 1° line BMT or IST; (n=7434)




EBMT SAA WP
C Dufour R Peffaults
A Risitano MT Van Lint
J Marsh G Socie
H Schrezenmeier J Passweg
IBMDR
N Sacchi
S Pollicheni
Data Center
Rosi Oneto
Cone nebula
EBMT
CENTERS