APLASTIC ANEMIA: bone marrow transplantation

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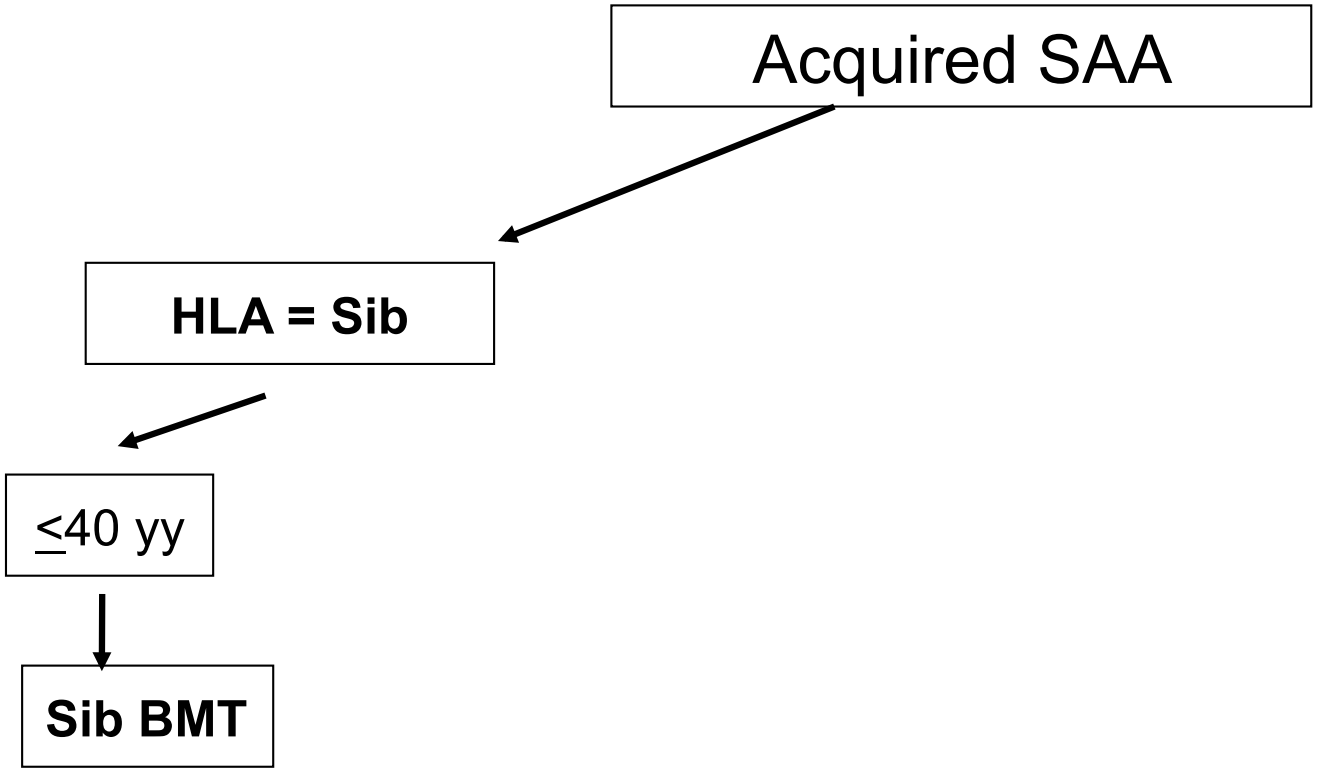
Rome , Italy


Acquired SAA
HLA = Sib
≤40 yy
Sib BMT

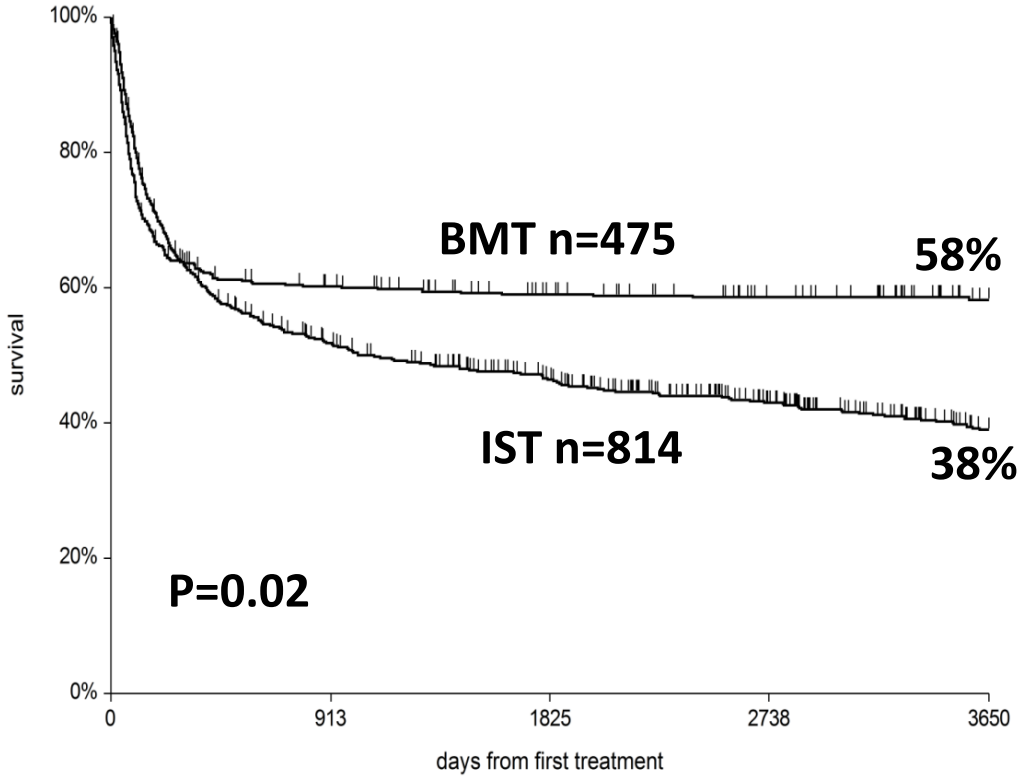
EVENT FREE SURVIVAL

Age <20 , VSAA /SAA

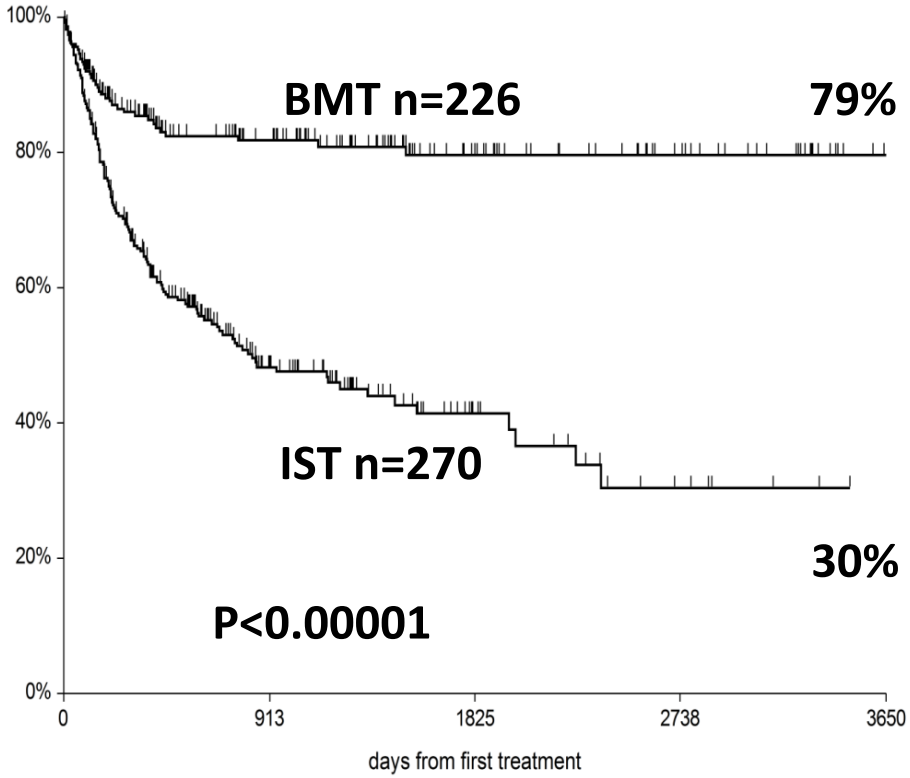
Event IS : death or BMT

BMT: death or ext-cGvHD

1976 - 1998



1999 - 2009



 # SAA <20 with an identical sibling , BMT first line

CY 200 +ATG is standard of care

First line HLA identical sibling BMT for SAA; (EBMT 2001-2010)

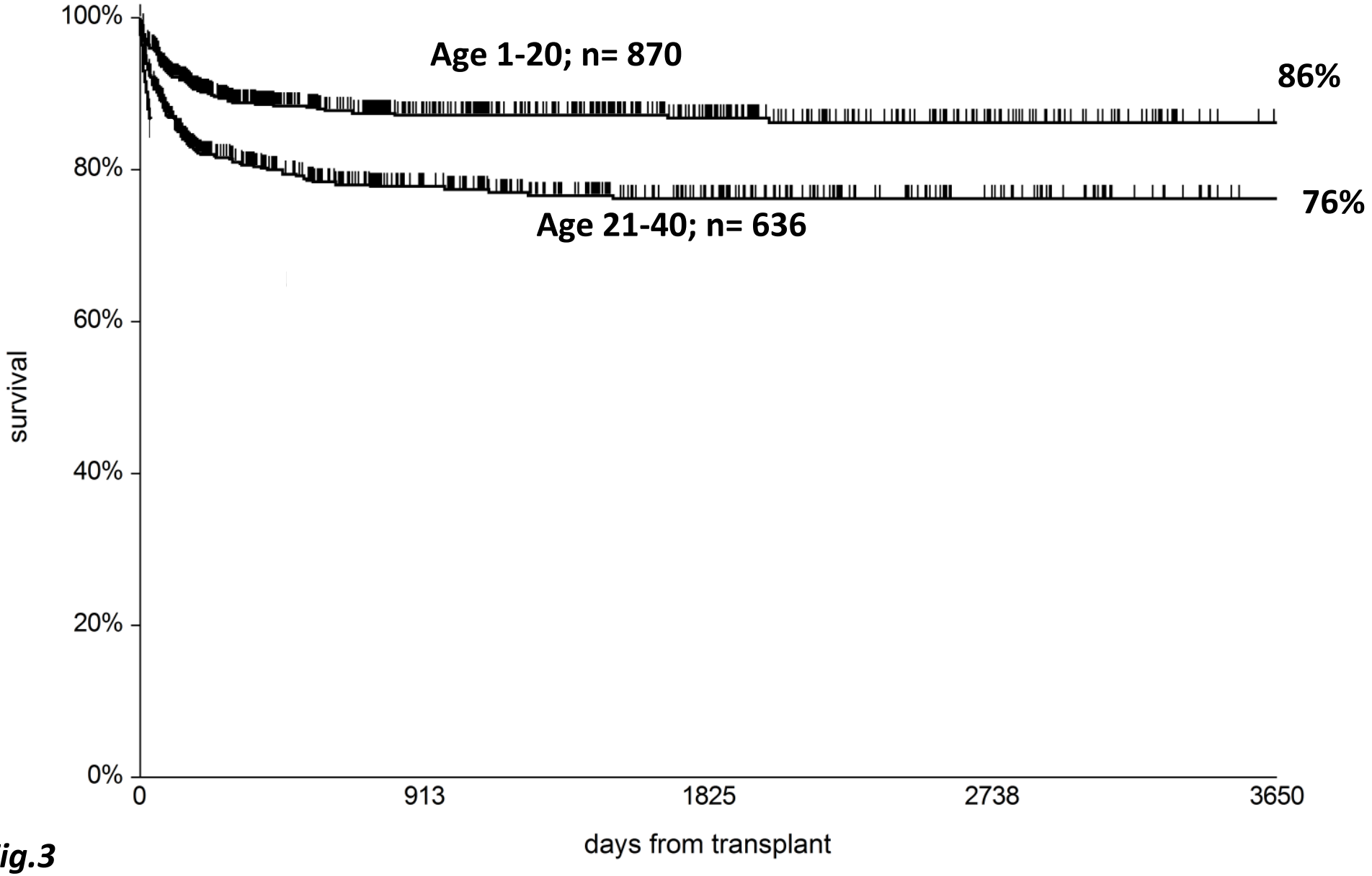


Fig.3

 # SAA <20 with an identical sibling , BMT first line

 # SAA 21-40 : id SIB BMT first line; conditioning to be optimized (CY 200 +ATG / FCC / FCA)

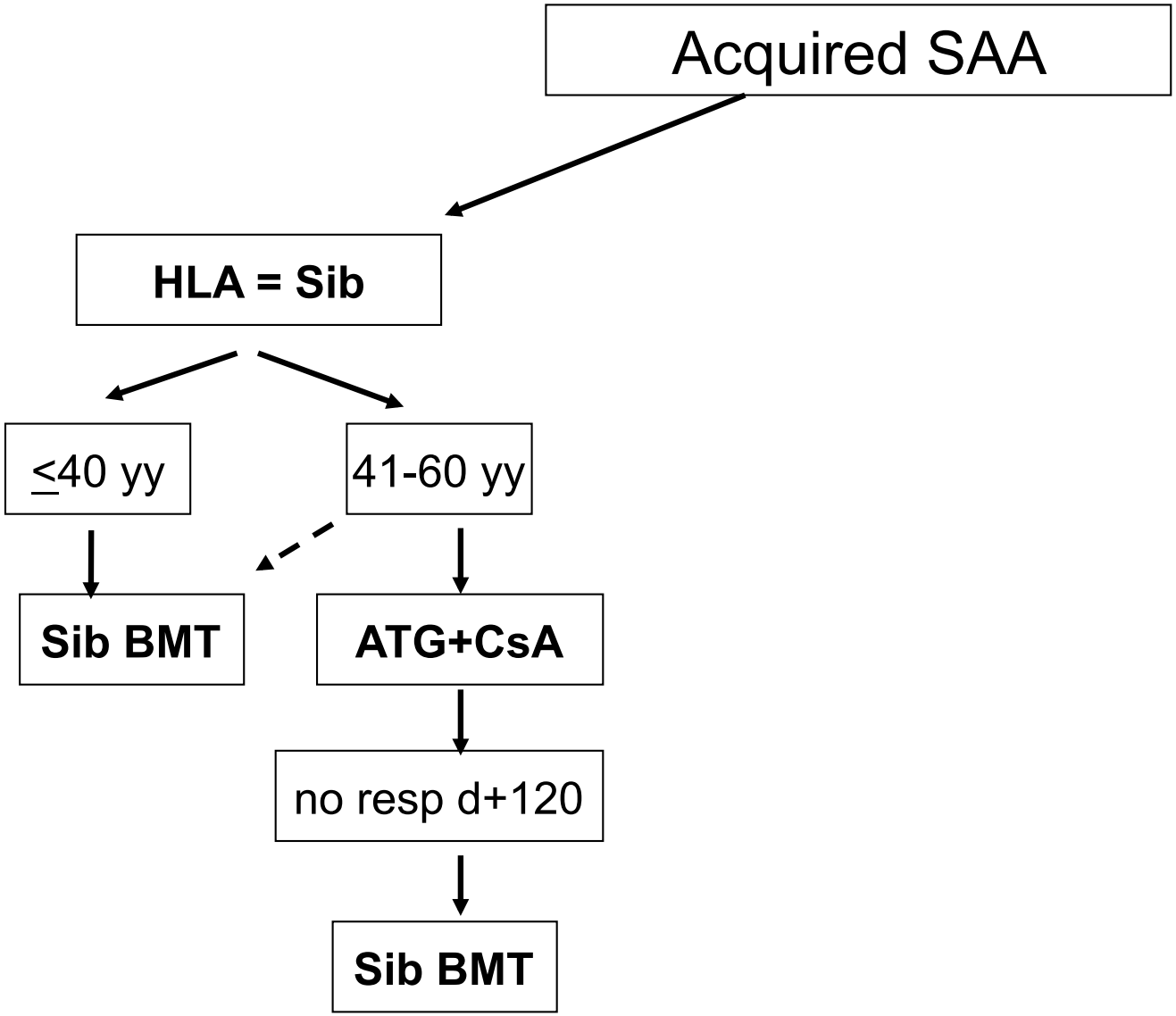

Acquired SAA
HLA = Sib
≤40 yy
41-60 yy
Sib BMT
ATG+CsA
no resp d+120
Sib BMT

Fig.2

SAA
HLA id sibs ; 2001-2010

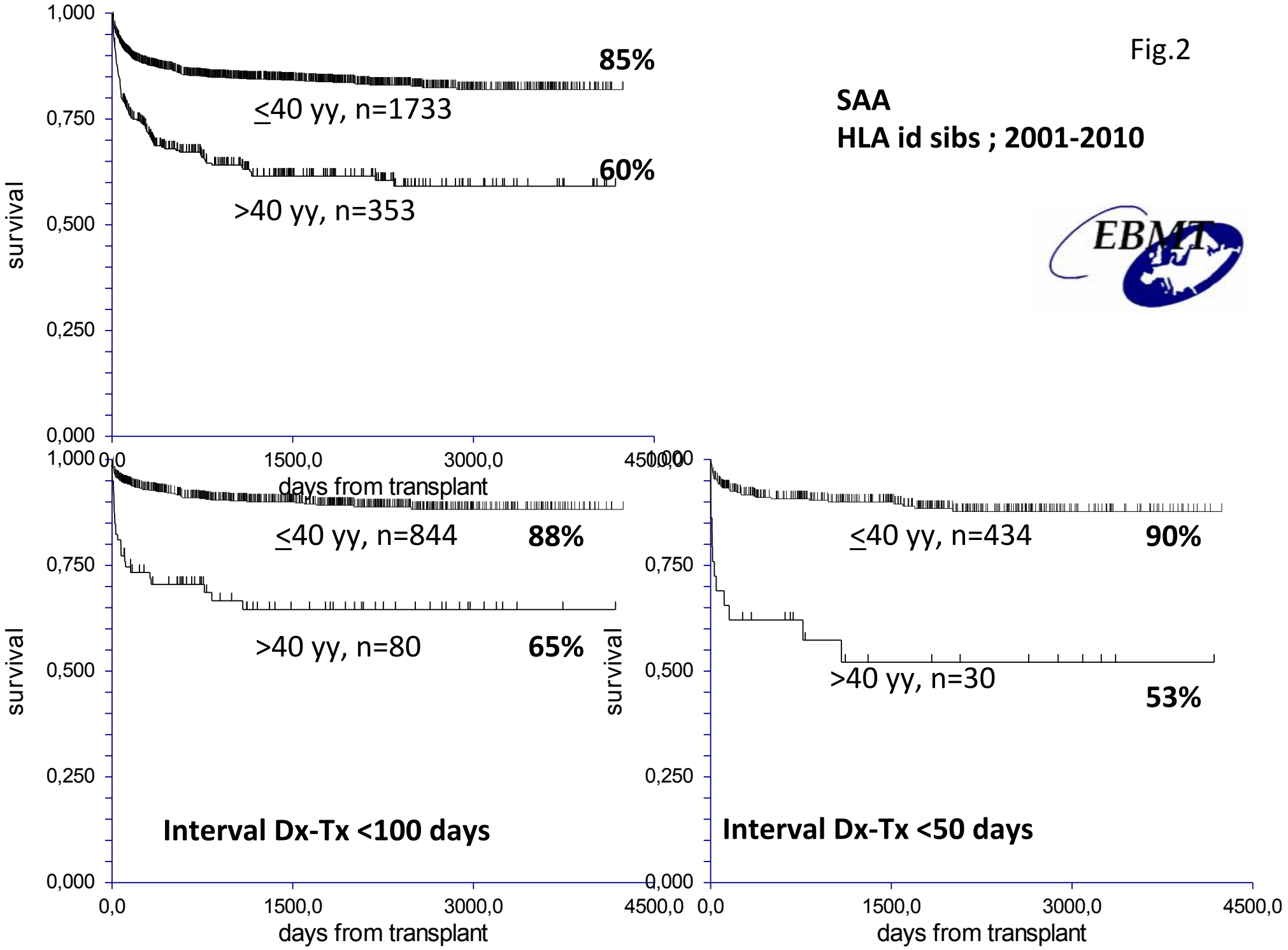
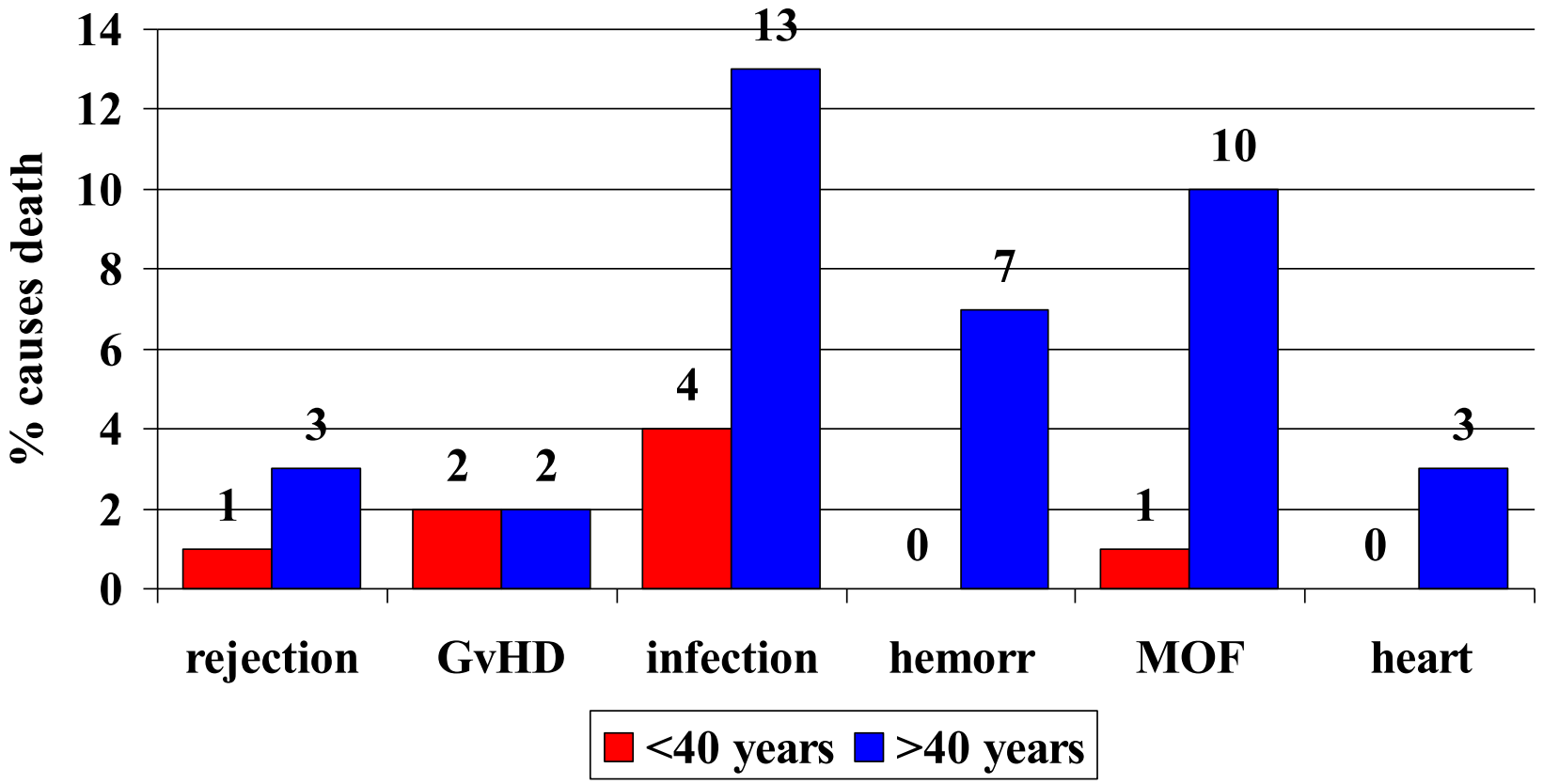


Fig.3

SAA HLA id siblings; 2001-2010
causes of death

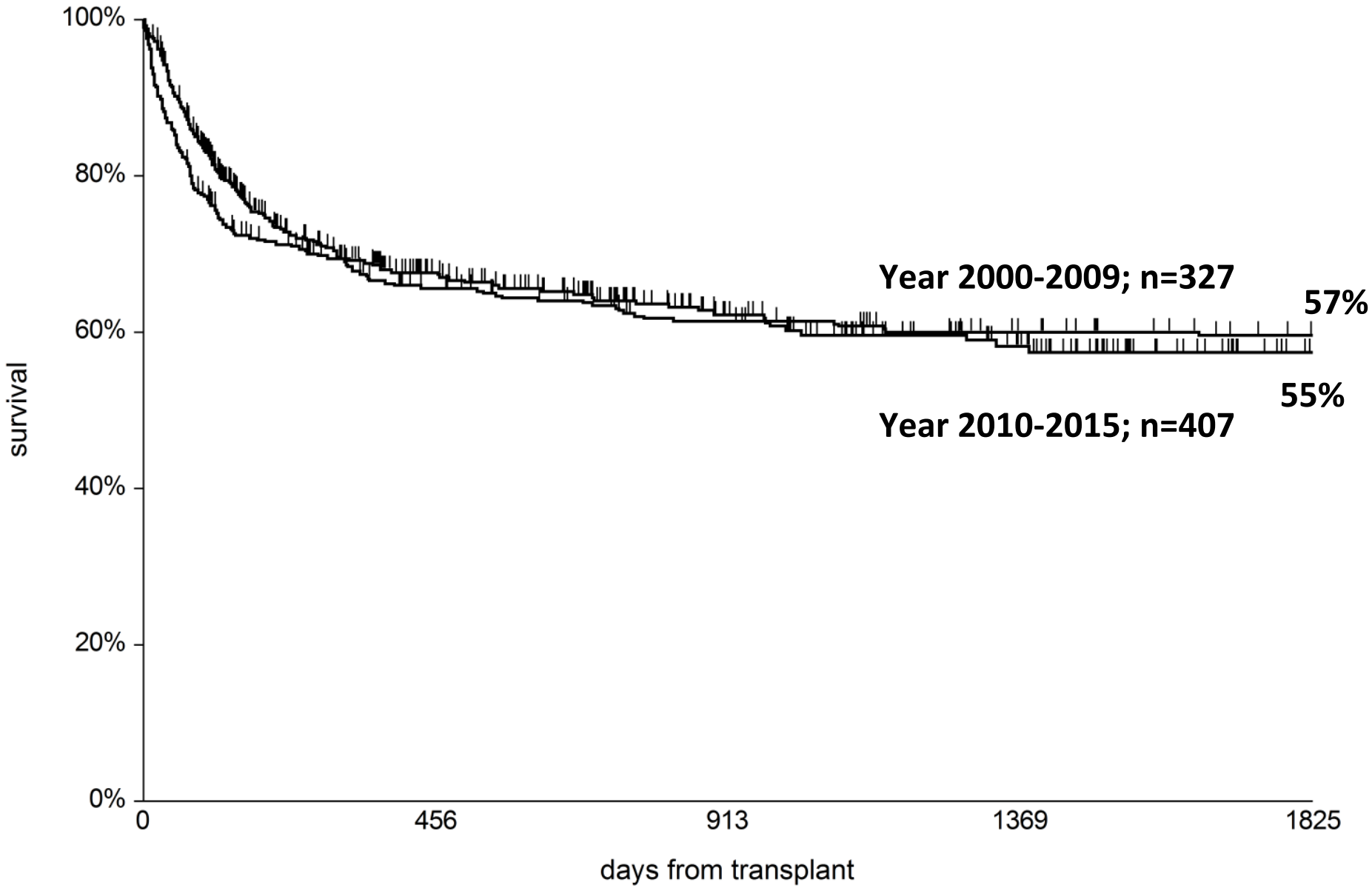


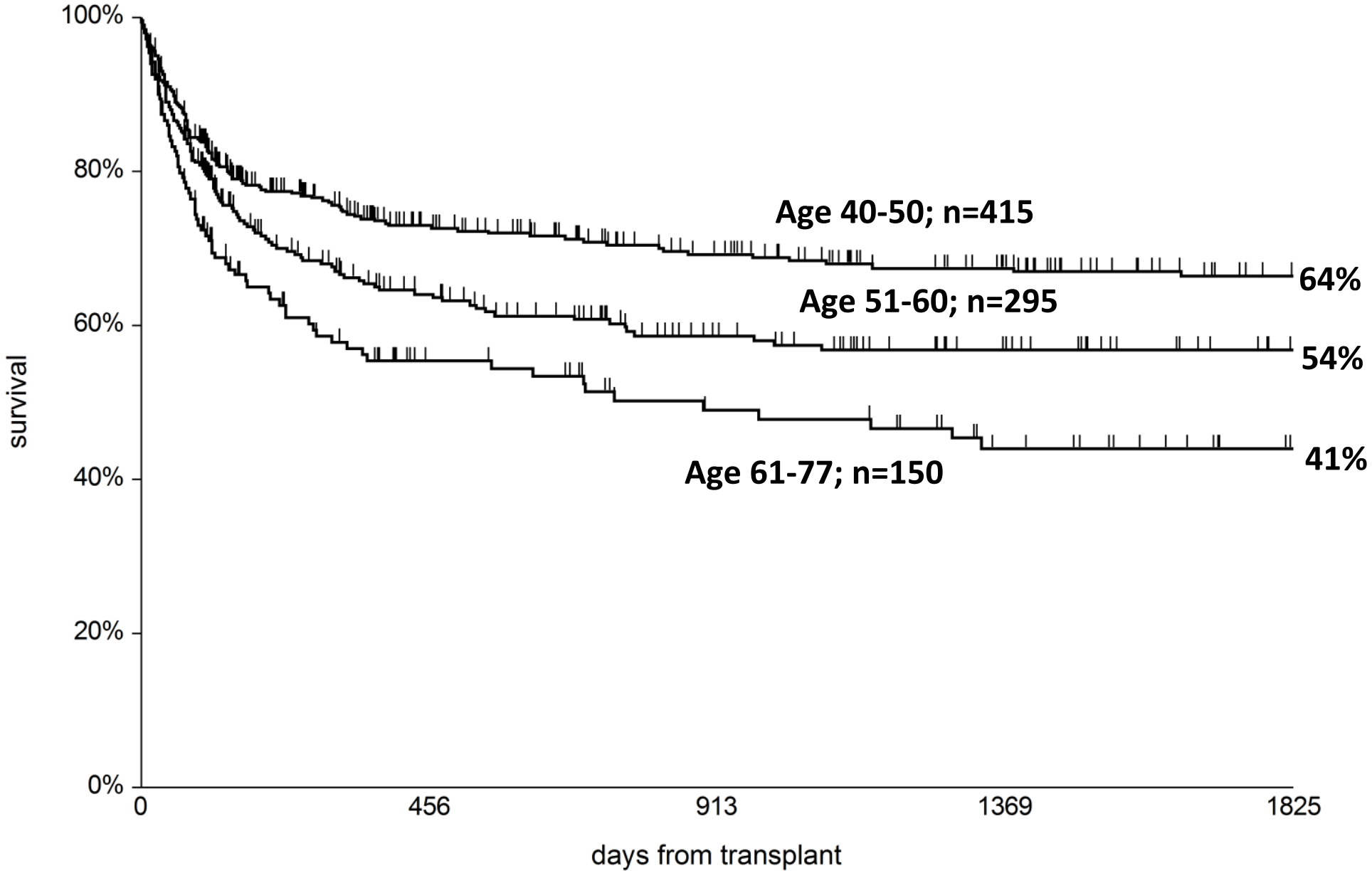
old data: in 2015 things have changed (yes?)

BMT for acquired SAA > 40 years of age

	2001-2010	2010-2015	
N=	327	427	
Age (med)	49 yy	53 yy	p<0.01
Alt donors	43%	64%	p<0.01
SC source	BM 41%	54%	p<0.01
FLU cont reg	42%	55%	p<0.01

Outcome of acquired SAA aged ≥ 40 years : median 50 yy (40-77)




100%
80%
60%
40%
20%
0%
survival
0
456
913
1369
1825
days from transplant
Age 40-50; n=415
64%
Age 51-60; n=295
54%
Age 61-77; n=150
41%

 # Age > 40 remains a significant risk factor for HLA id BMT, also in 2015

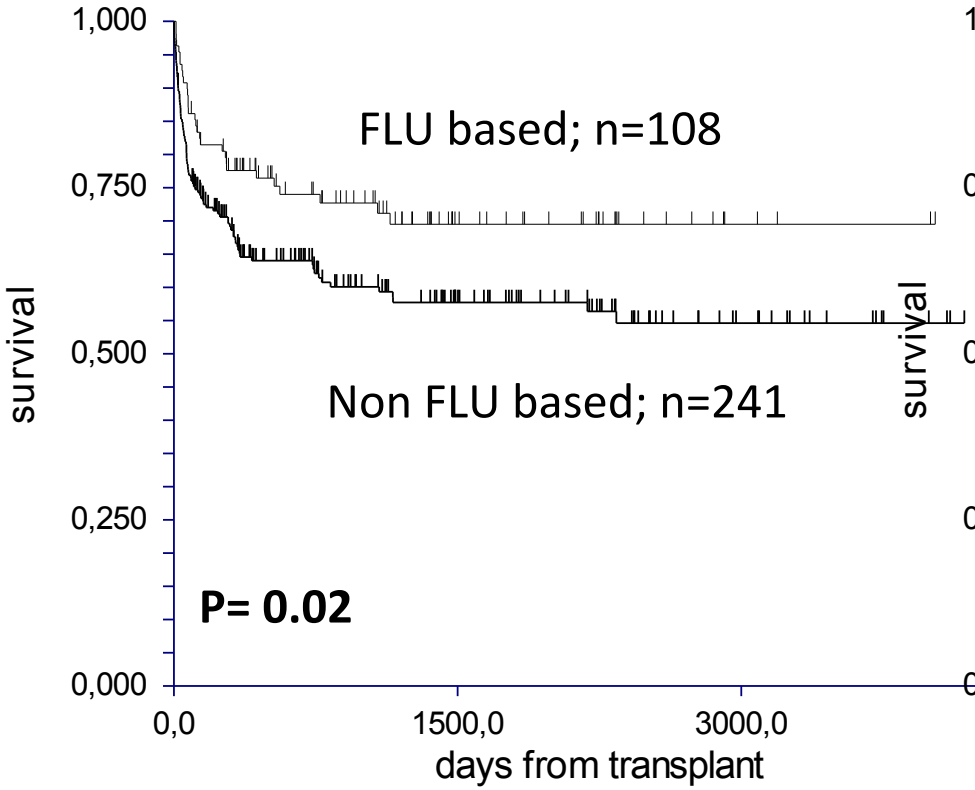
 # ATG+CyA (+EPAG?) should be first line therapy in acquired SAA > 40 years

 # The strong age effect persists >40 >50 >60 years

 # old data: in 2015 things have changed (yes?)
 # can we improve the conditioning for SAA in pts over 40 years?

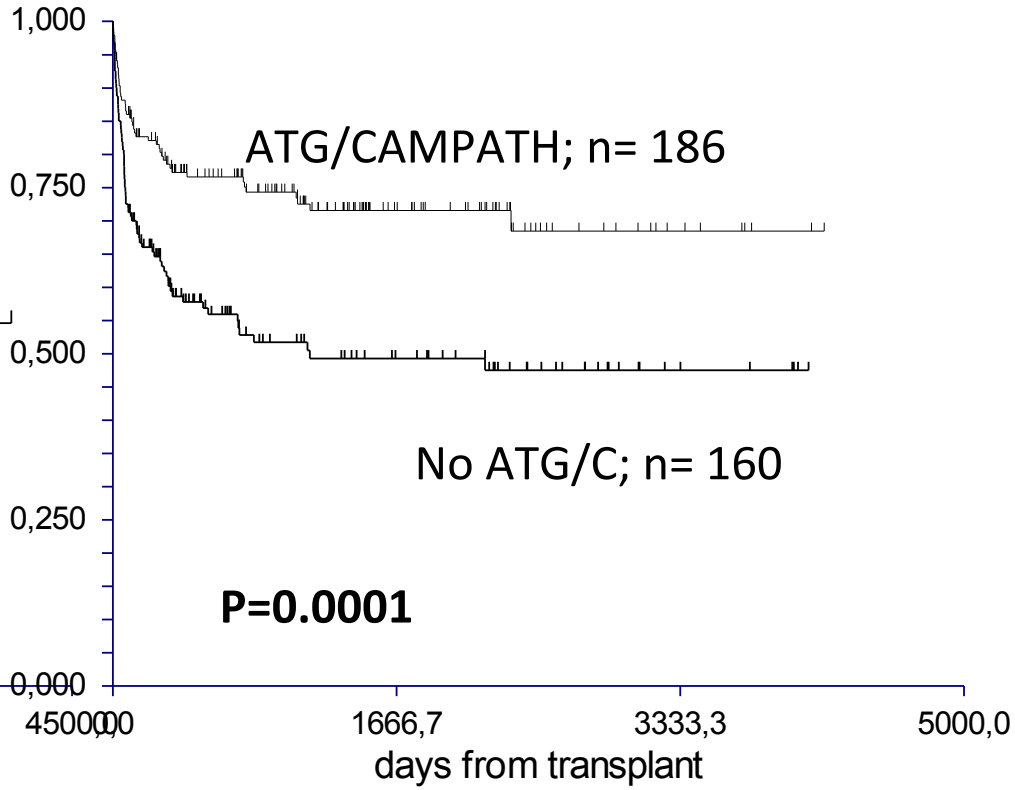
SAA 2001-2010

HLA= SIB , Age > 40 years

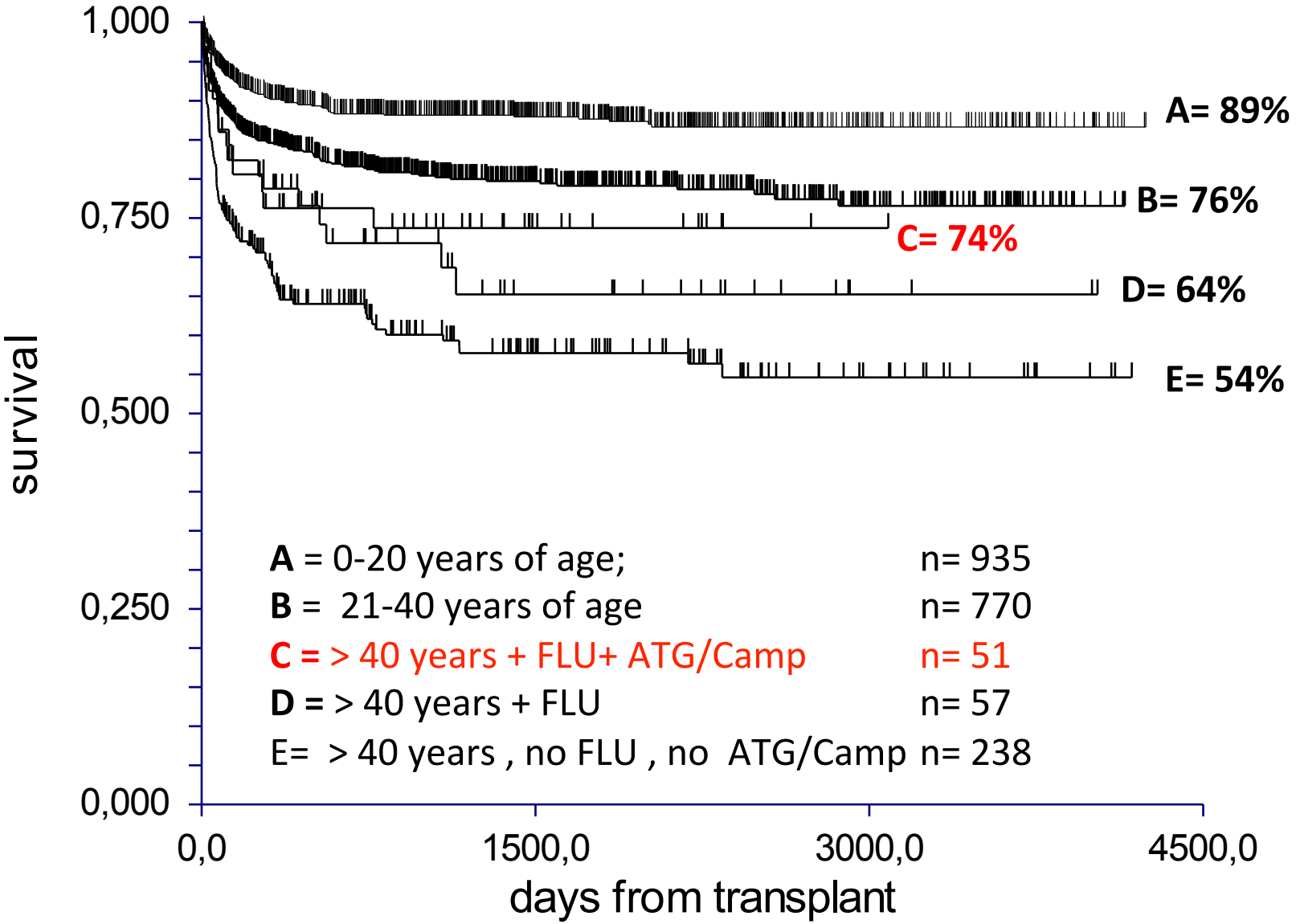


SAA 2001-2010

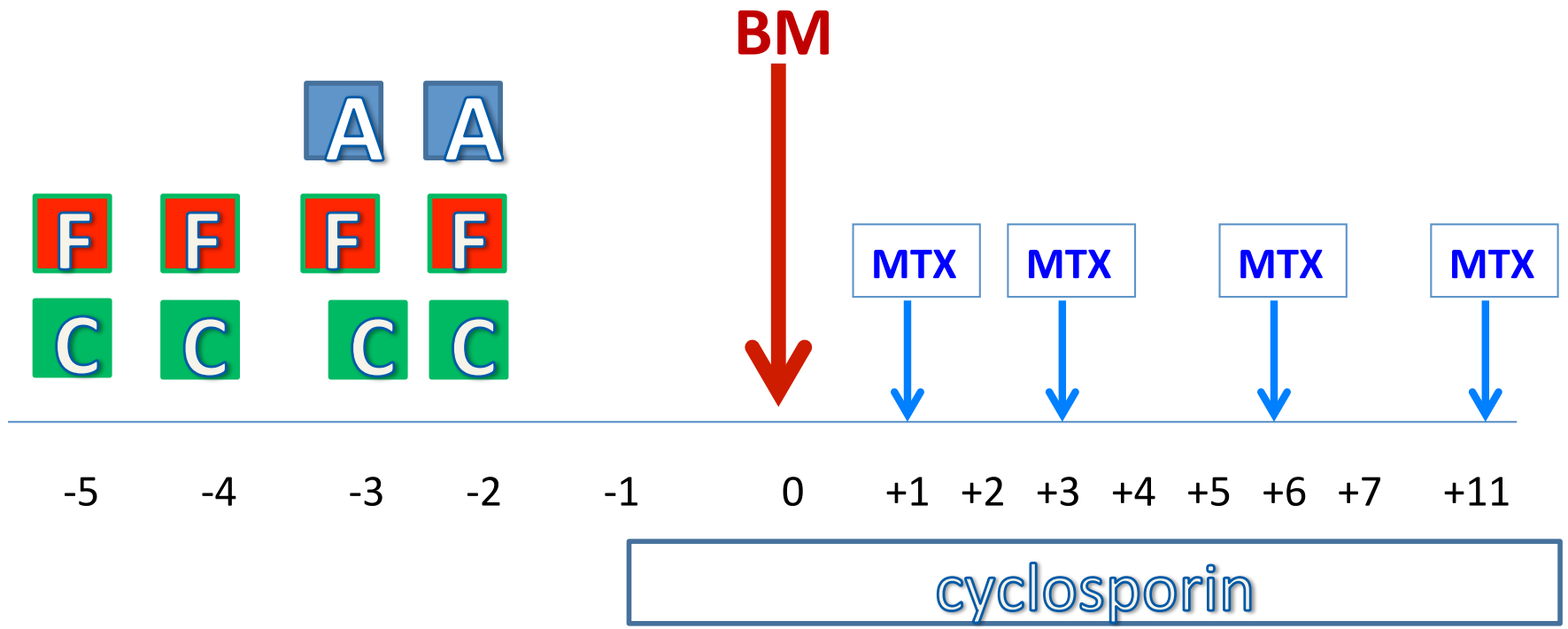
HLA = SIB > 40 years



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



conditioning regimen for SIB transplants in acquired SAA > age of 40

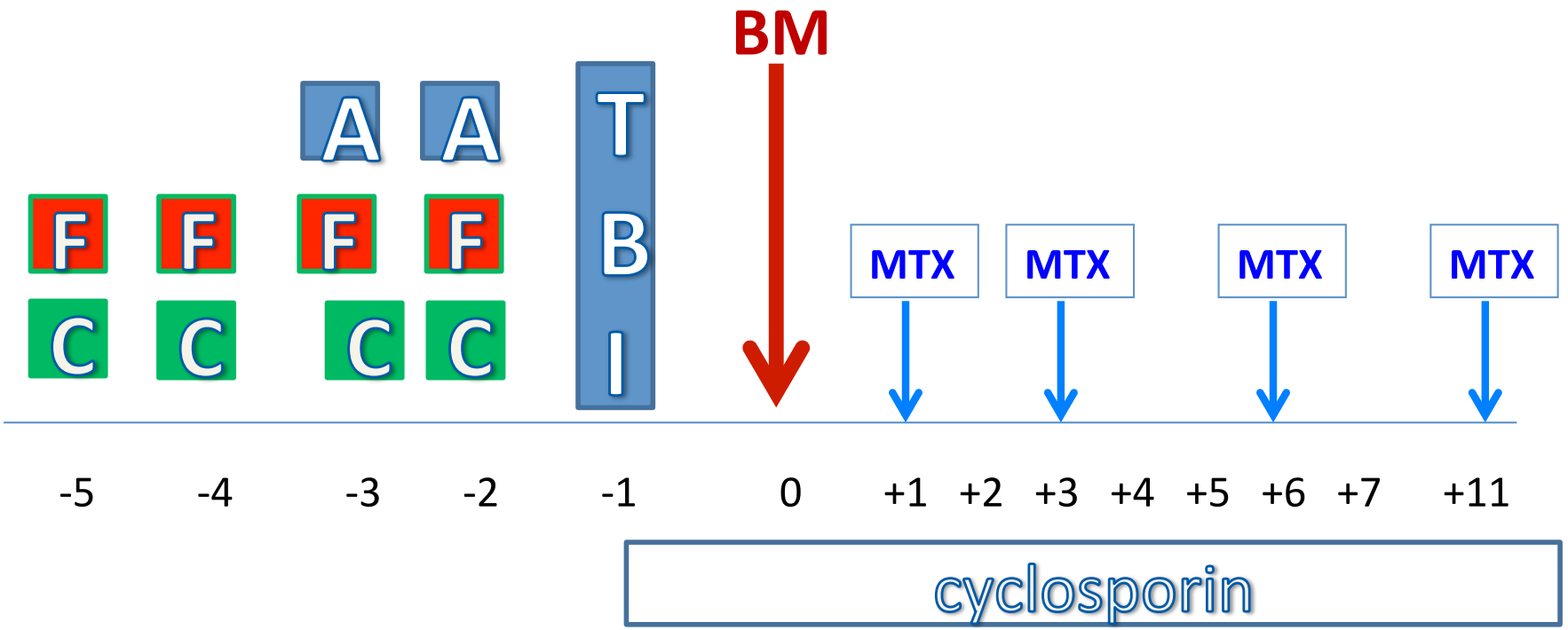


F **FLUDARABINE 30 mg/m^2/day x4**

C **CYCLOPHOSPHAMIDE 30 mg/kg/day x4**

A **ATG : 3.75 mg/kg/day (or CAMPATH 20 mg/day x5)**

conditioning regimen for SIB transplants in acquired SAA > age of 40



F **FLUDARABINE 30 mg/m^2/day x4**

C **CYCLOPHOSPHAMIDE 30 mg/kg/day x4**

A **ATG : 3.75 mg/kg/day**

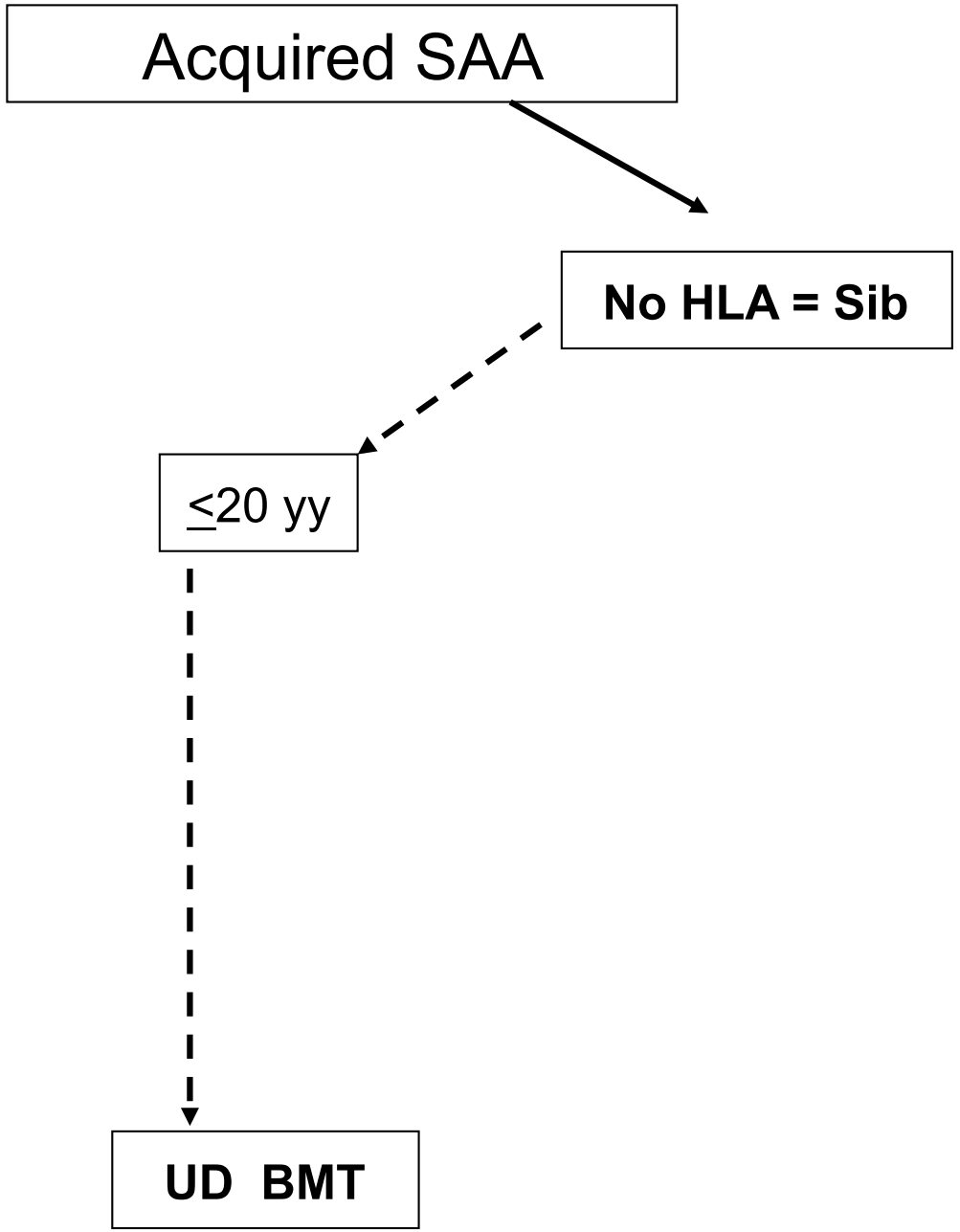
TBI **Total body irradiation 2 Gy for sensitized patients**

Conditioning regimen SIB transplants

Young patients (<20 yy) CY200 +ATG

Older patients FLU CY ATG (± TBI 2)/ FCC

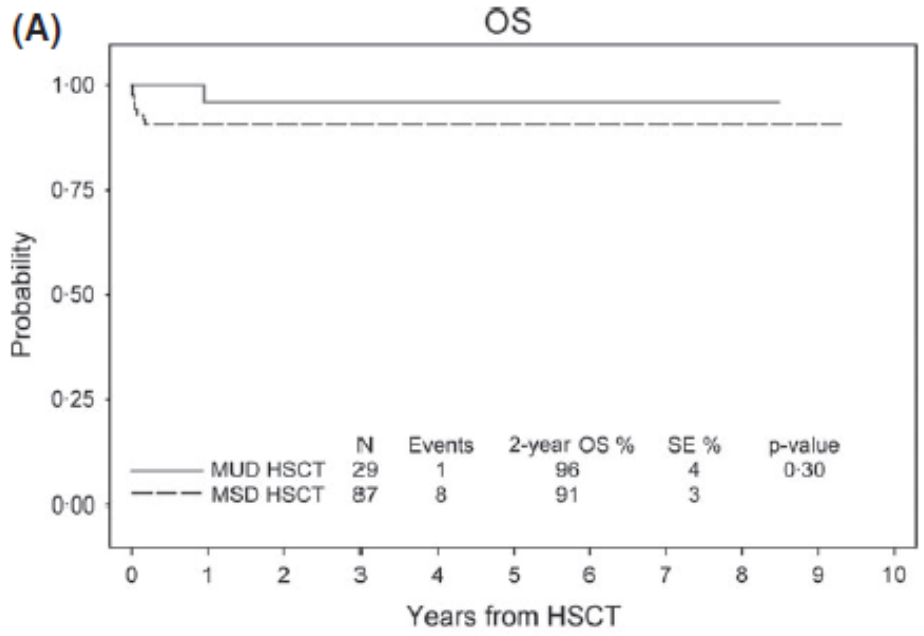
old data: in 2015 things have changed (yes?)
can we improve the conditioning for SAA in pts over 40 years?
 # and Unrelated Transplants?

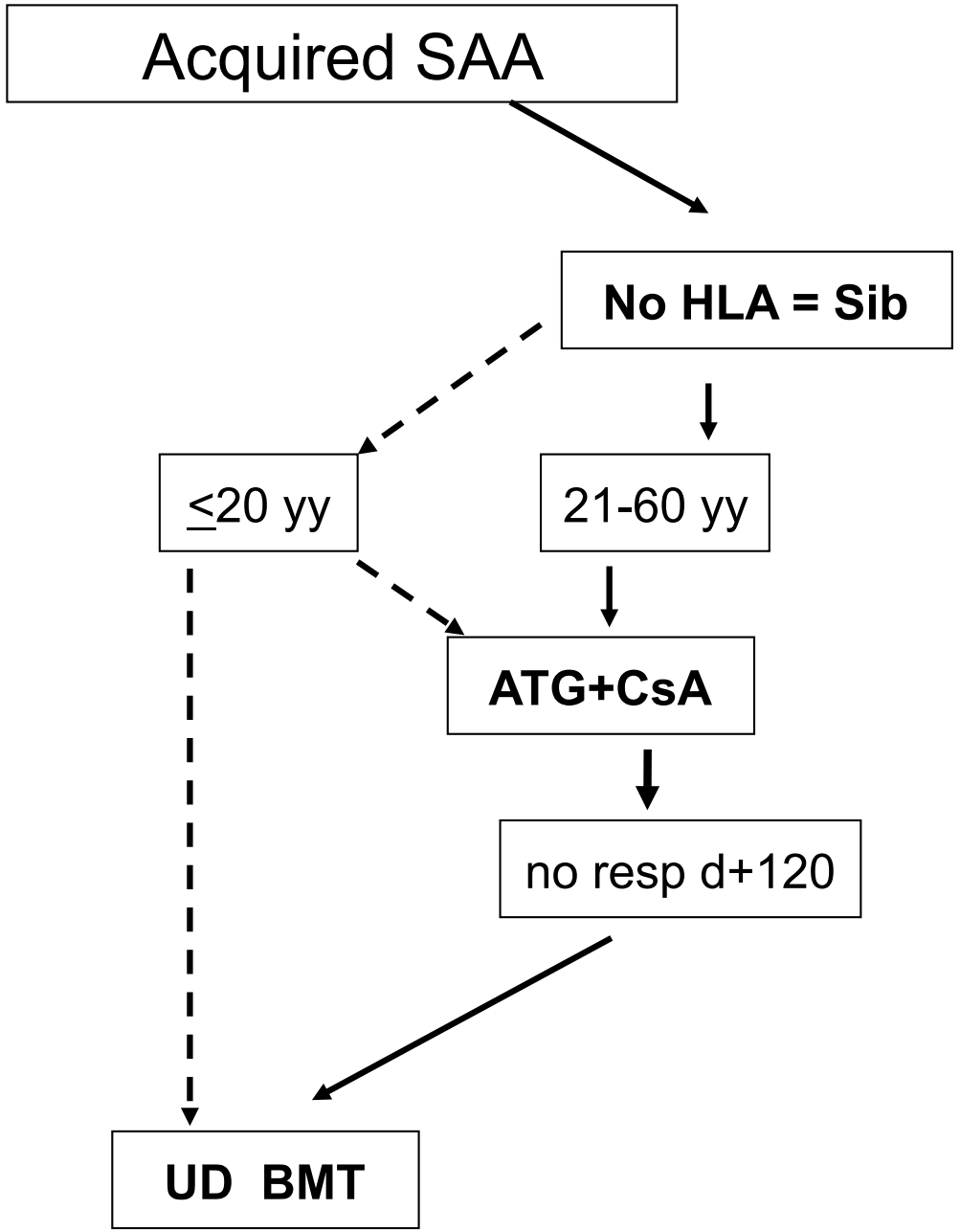

Acquired SAA
No HLA = Sib
≤20 yy
UD BMT

bjh research paper

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

British Journal of Haematology, 2015, **171**, 585–594




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

old data: in 2015 things have changed (yes?)
can we improve the conditioning for SAA in pts over 40 years?
and Unrelated Transplants?
 # best conditioning regimen ?

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

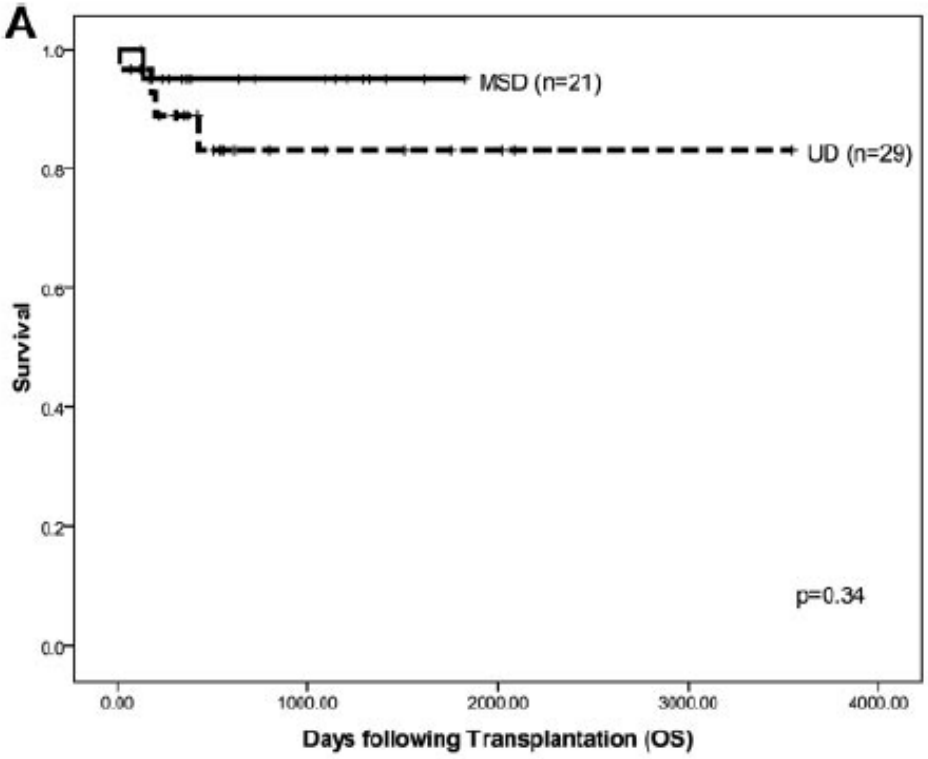
Alemtuzumab with fludarabine and cyclophosphamide reduces chronic graft-versus-host disease after allogeneic stem cell transplantation for acquired aplastic anemia

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

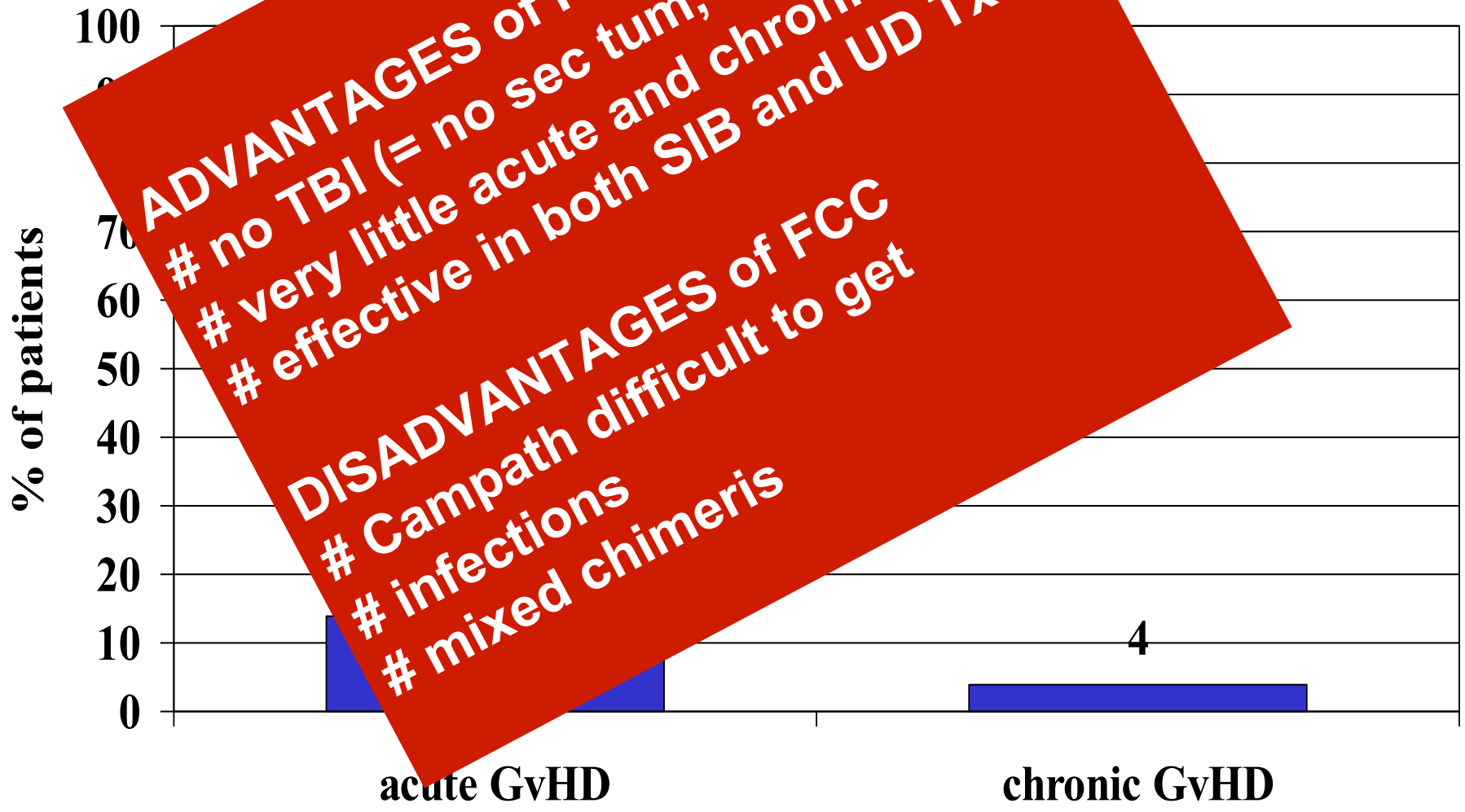
FCC (FLU CY CAMP 100)
UD n=29
SIB n=21

Age 35 (8-62)
DxTX 6mm (SIB) 10mm (UD)

BM(24) PB(14) GBM(7)
BM+PB (5)



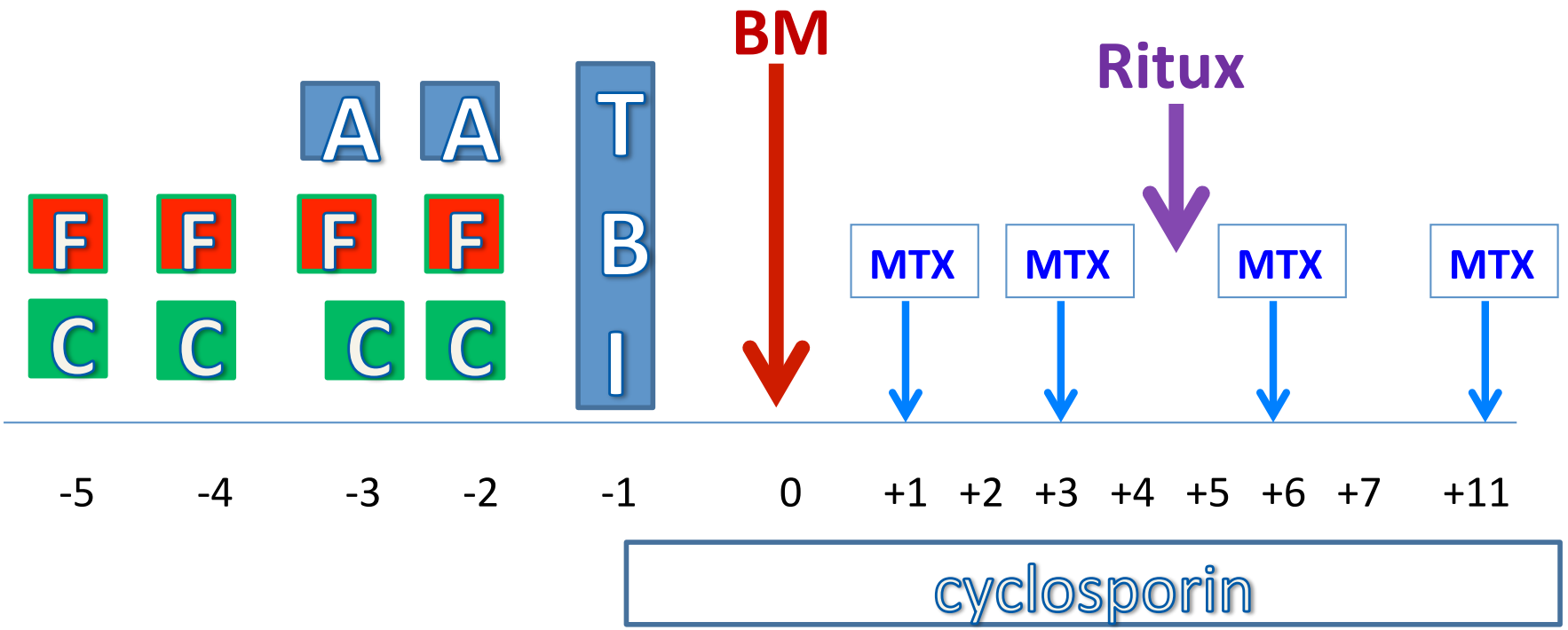
FCC for aplastic anemia (P



ADVANTAGES of FCC
no TBI (= no sec tum, infertility)
very little acute and chronic GvHD
effective in both SIB and UD Tx

DISADVANTAGES of FCC
Campath difficult to get
infections
mixed chimeris

conditioning regimen for UD transplants in acquired SAA: EBMT



F FLUDARABINE 30 mg/m^2/day x4

C CYCLOPHOSPHAMIDE 30 mg/kg/day x4

A ATG : 3.75 mg/kg/day

TBI Total body irradiation 2 Gy

Ritux= 200 mg

Fludarabine, cyclophosphamide, antithymocyte globulin, with or without low dose total body irradiation, for alternative donor transplants, in acquired severe aplastic anemia: a retrospective study from the EBMT-SAA working party

Andrea Bacigalupo,[1] Gerard Socie',[2] Edoardo Lanino,[3] Arcangelo Prete,[4] Franco Locatelli,[5] Anna Locasciulli,[6] Simone Cesaro,[7] Avichai Shimoni,[8] Judith Marsh,[9] Mats Brune,[10] Maria Teresa Van Lint,[1] Rosi Oneto,[1] and Jacob Passweg[13] for the Severe Aplastic Anemia Working Party of the European Group for Blood and Marrow Transplantation (SAA WP-EBMT)

haematologica | 2010; 95(6)

Chronic GvHD

FCA	27%	ext 2%
FCA+TBI	50%	ext 8%

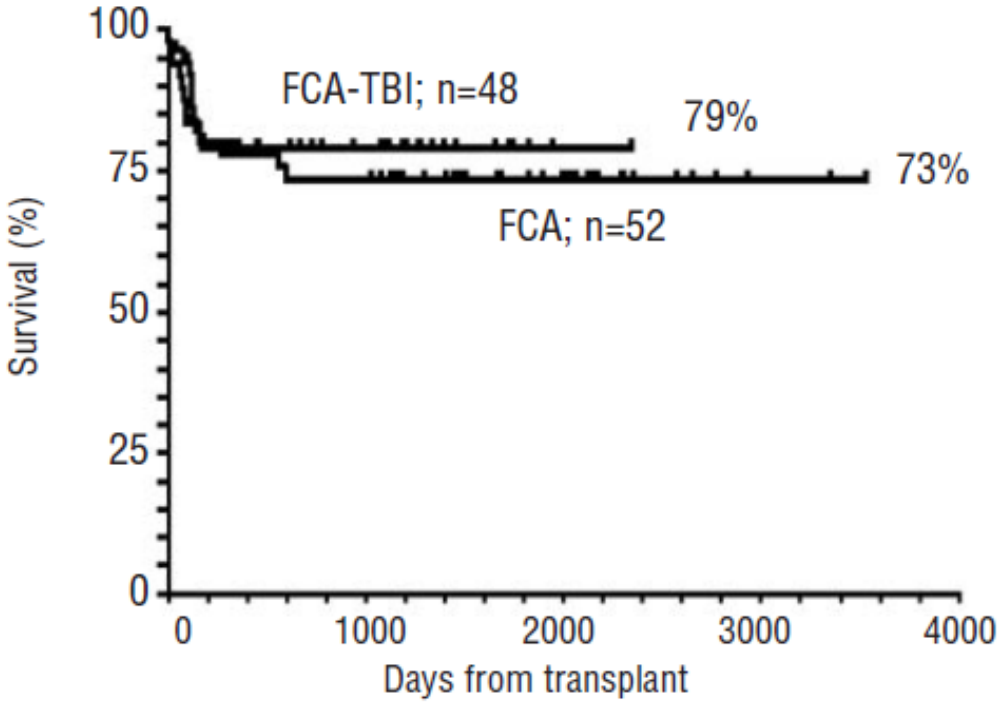


Figure 1. Actuarial survival of 52 SAA patients receiving FCA and 48 SAA patients receiving FCA + 2Gy TBI.

Conditioning regimen UD transplants

FLU CY CAMPTH (UK)

FLU CY ATG +TBI 2Gy (EBMT-USA-JAPAN)

old data: in 2015 things have changed (yes?)
can we improve the conditioning for SAA in pts over 40 years?
and Unrelated Transplants?
best conditioning regimen ?
 # how do UD compare with SIB transplants?

Bone Marrow Transplantation (2010) 45, 1508–1513

www.nature.com/bmt

ORIGINAL ARTICLE

Comparison of matched-sibling donor BMT and unrelated donor BMT in children and adolescent with acquired severe aplastic anemia

H Yagasaki[1], Y Takahashi[1], A Hama[1], K Kudo[1], N Nishio[1], H Muramatsu[1], M Tanaka[1], N Yoshida[1], K Matsumoto[2], N Watanabe[3], K Kato[2], K Horibe[3] and S Kojima[1]

N=61 treated at
1 single Institution

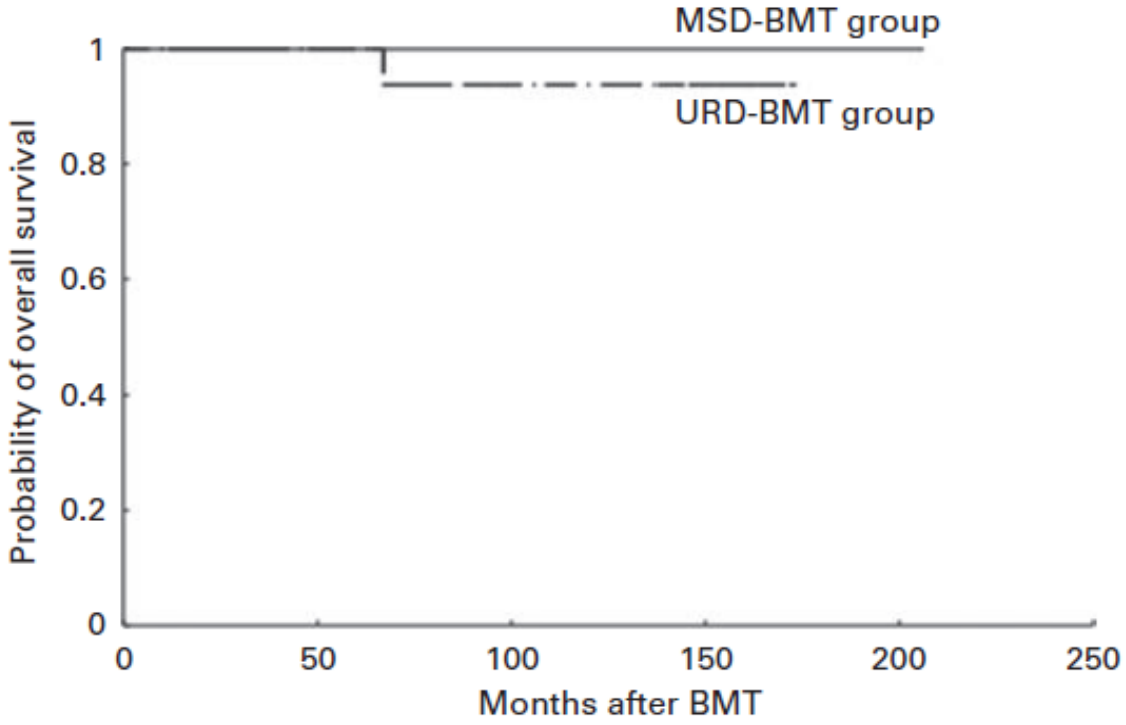


Figure 1 Kaplan–Meier estimates of OS after MSD-BMT and URD-BMT, respectively (100% vs 93.8%) ($P = 0.252$).

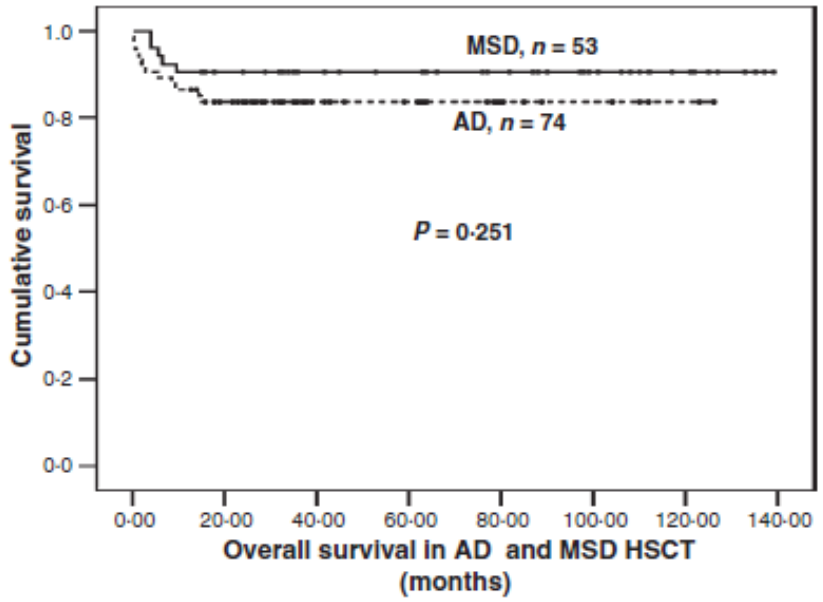
bjh research paper 2013

Allogeneic stem cell transplantation for children with acquired severe aplastic anaemia: a retrospective study by the Viva-Asia Blood and Marrow Transplantation Group

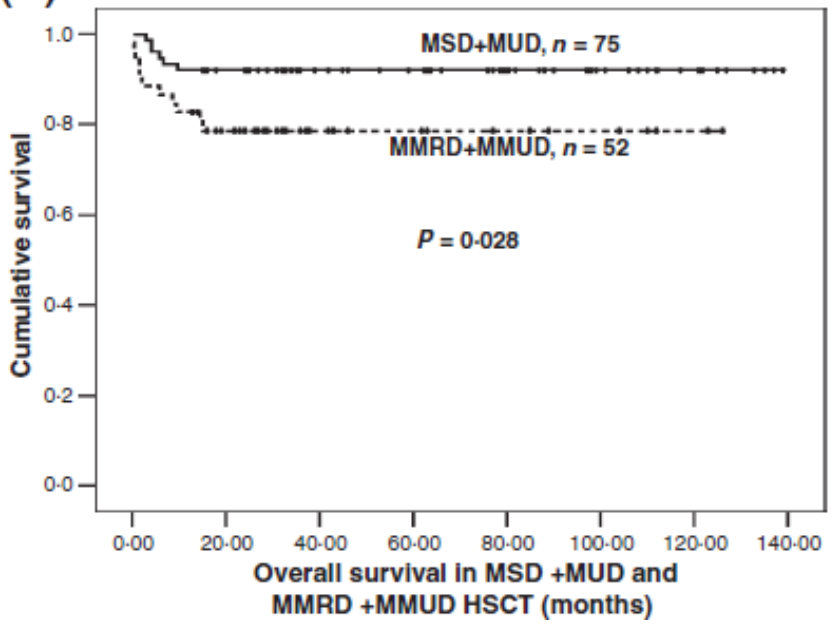
Jing Chen,[1] Vincent Lee,[2] Cheng Juan Luo,[1] Alan Kwok Shing Chiang,[3] Suradej Hongeng,[4] Poh Lin Tan,[5] Ah Moy Tan,[6] Kleebsabai Sanpakit,[7] Chun Fu Li,[8] Anselm Chi-wai Lee,[9] Hsin Chieh Chua[5] and Yasuhiro Okamoto[10]

127 children
MSD n=50
MUD n=22
mMUD n=32
mmFAM n=20

(C)



(B)

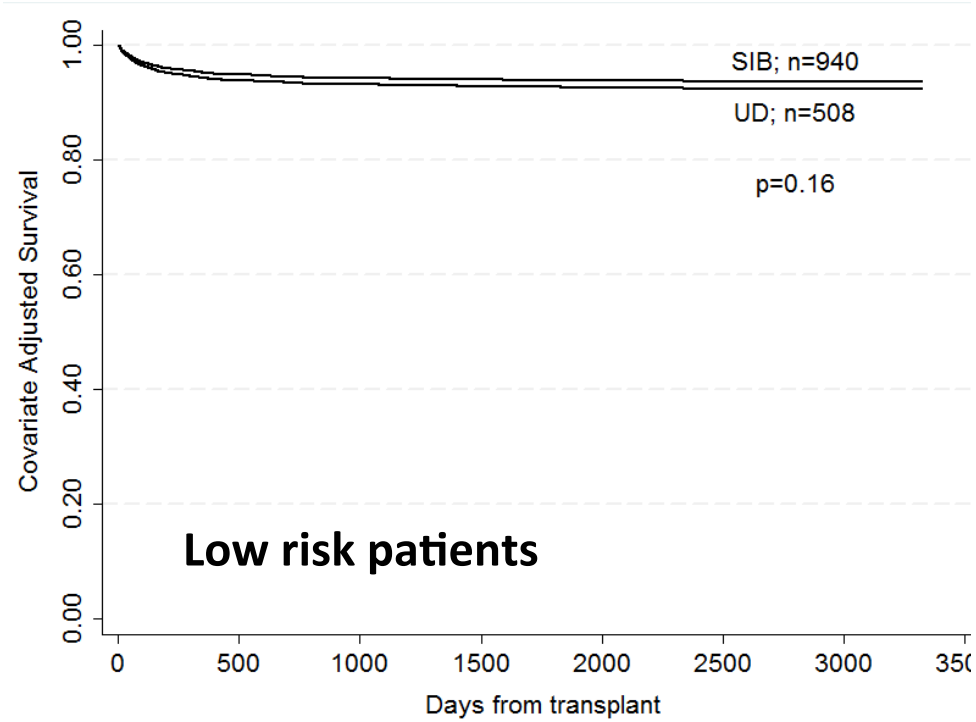


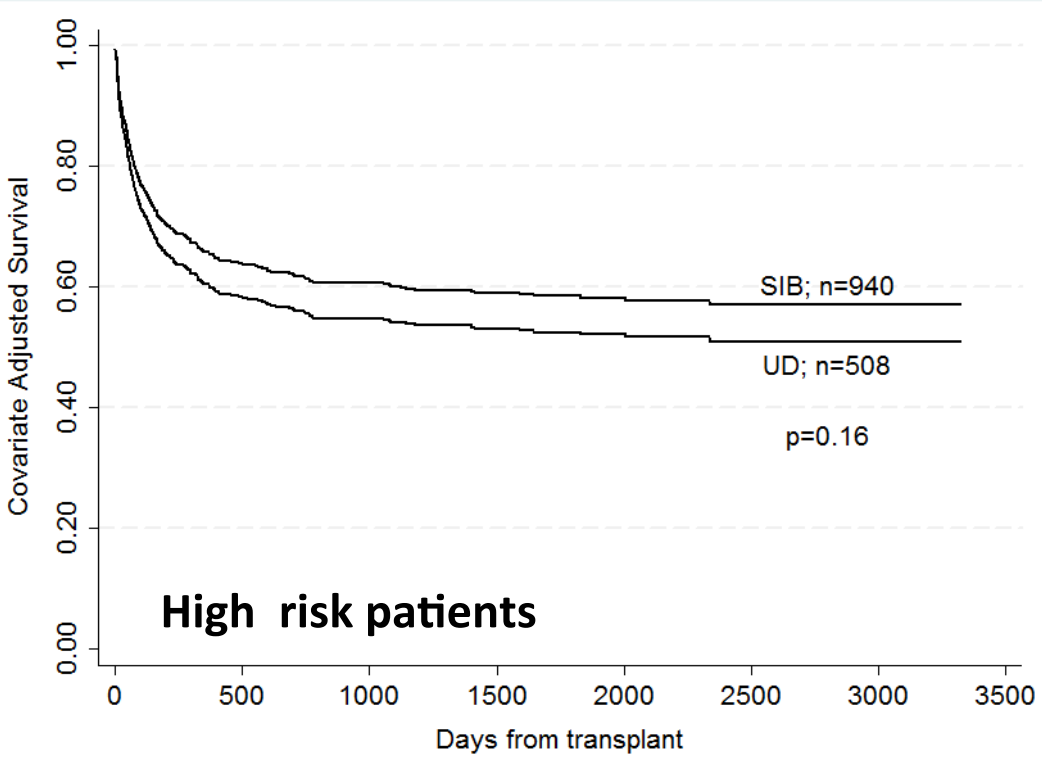
ALLOGENEIC TRANSPLANTS FOR APLASTIC ANEMIA

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

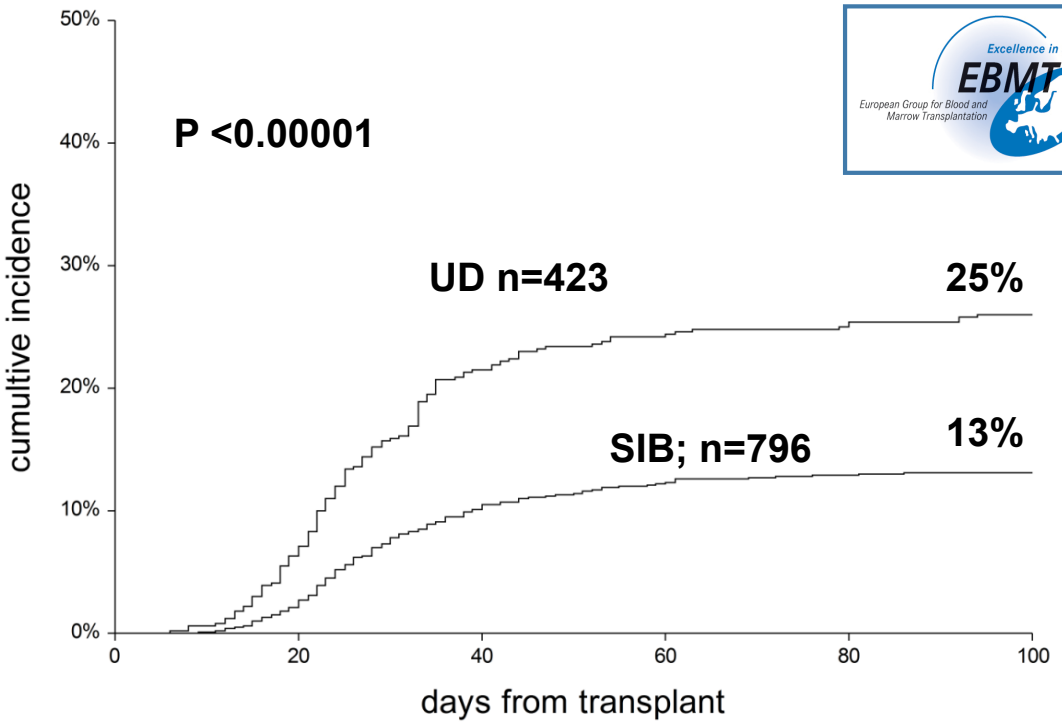
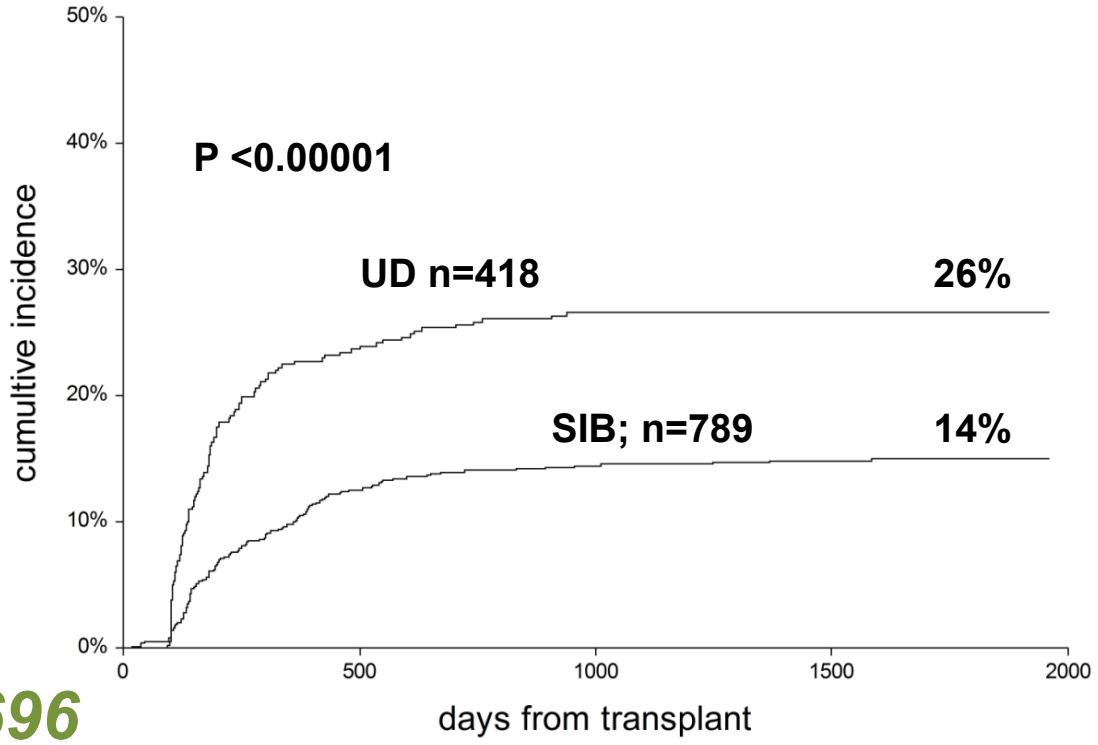


Fig. 1b Chronic GvHD

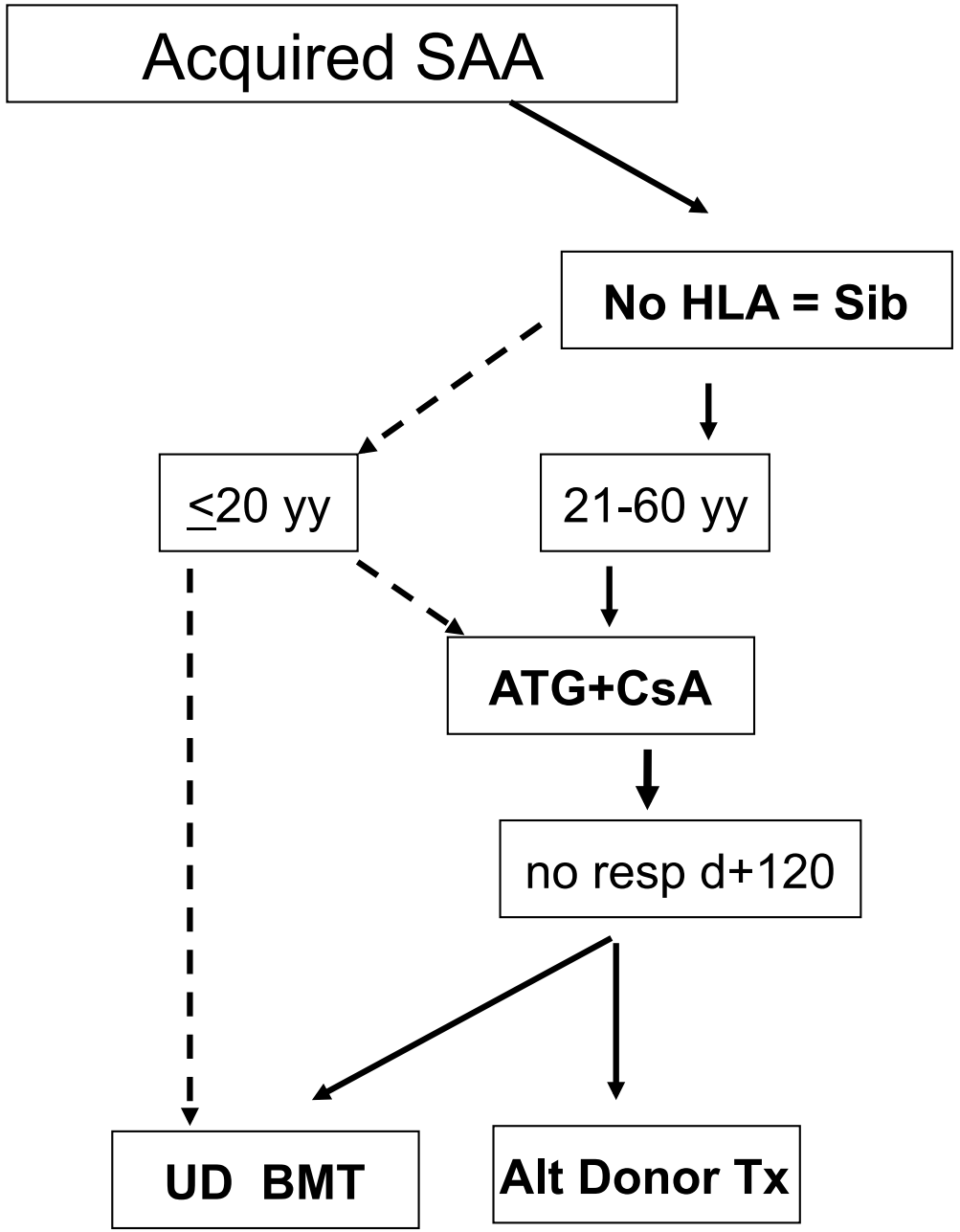


Haematologica 2015; 100; 696

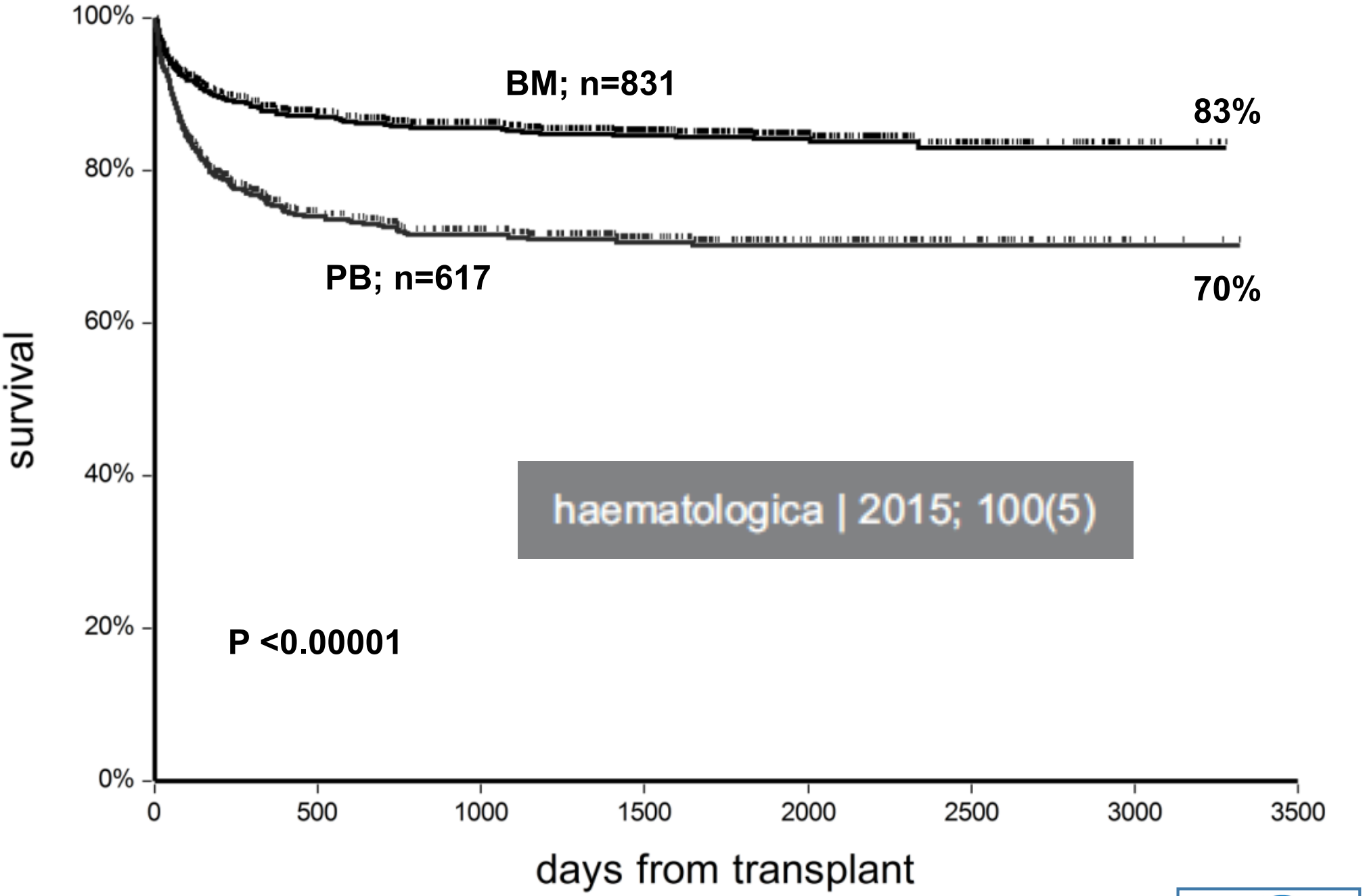
Outcome of UD and SIB transplants

For SAA

Currently almost superimposable
GvHD still more frequent in UD TX

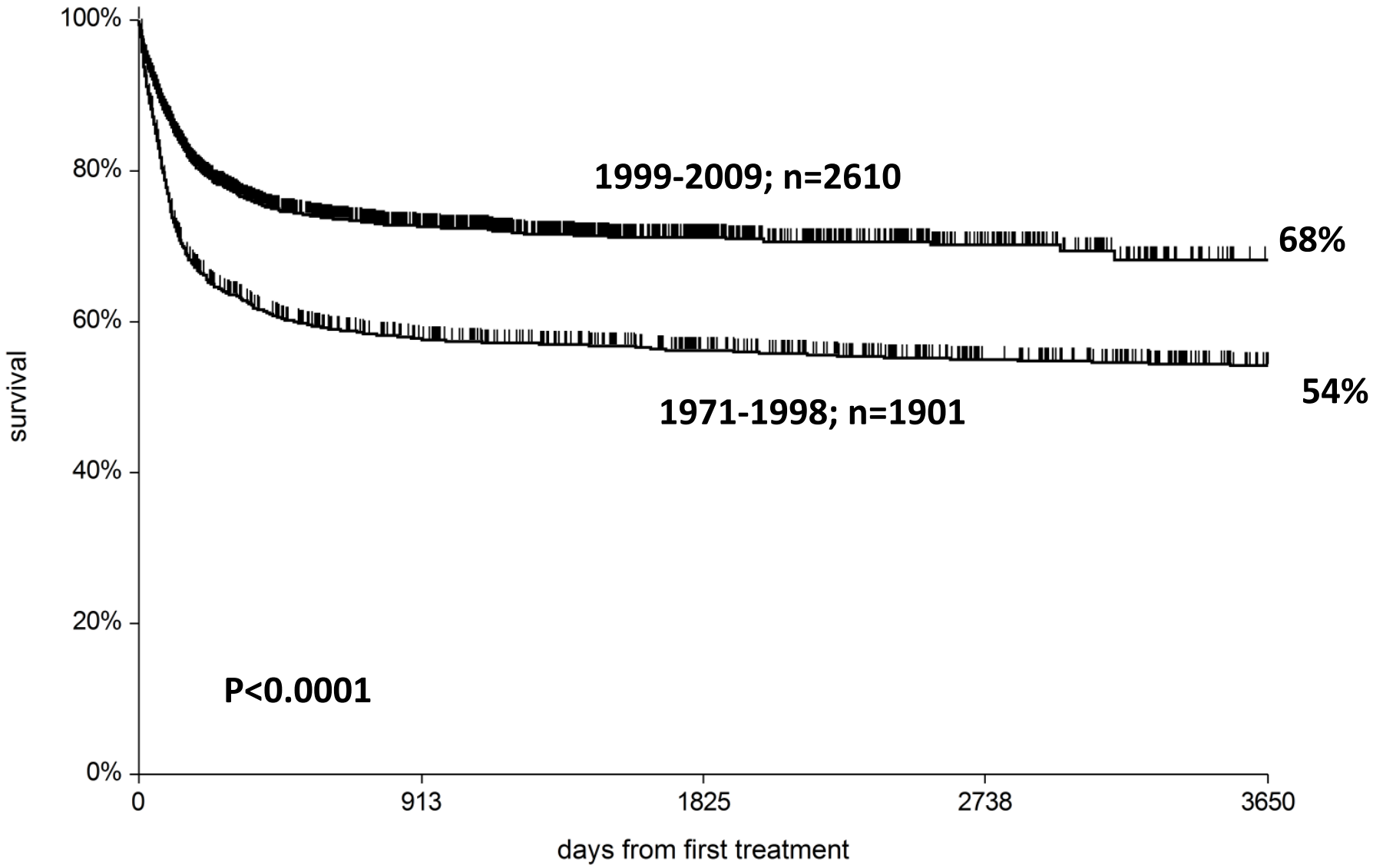

Acquired SAA
No HLA = Sib
≤20 yy
21-60 yy
ATG+CsA
no resp d+120
UD BMT
Alt Donor Tx

old data: in 2015 things have changed (yes?)
can we improve the conditioning for SAA in pts over 40 years?
and Unrelated Transplants?
best conditioning regimen ?
how do UD compare with SIB transplants?
 # stem cell source?


100%
80%
60%
40%
20%
0%
survival
BM; n=831
83%
PB; n=617
70%
haematologica | 2015; 100(5)
P <0.00001
0
500
1000
1500
2000
2500
3000
3500
days from transplant

old data: in 2015 things have changed (yes?)
can we improve the conditioning for SAA in pts over 40 years?
and Unrelated Transplants?
best conditioning regimen ?
how do UD compare with SIB transplants?
stem cell source?
 # have results improved overall?

BONE MARROW TRANSPLANTATION



Excellence in science
EBMT
European Group for Blood and Marrow Transplantation

CONCLUSIONS

40 years is still an age cut-off
there is a need for improvement in patients over 40: test prospectively 2 conditioning regimens
UD and SIB BMT now «almost» superimposable
BM remains the standard SC source
significant overall improvement of survival for BMT in SAA


GITMO Centers
LMC
EBMT WPSAA
C Dufour A Risitano
J Marsh J Passweg
H Schrezenmeier
G Socie' MT Van Lint
A Tichelli A Locasciulli
SMC
Nursing Staff
IBMDR
N Sacchi
Data Center
Rosi Oneto