Fanconi Anemia Research Fund
Annual Family Meeting 2011

Camp Sunshine, June 24-28, 2011

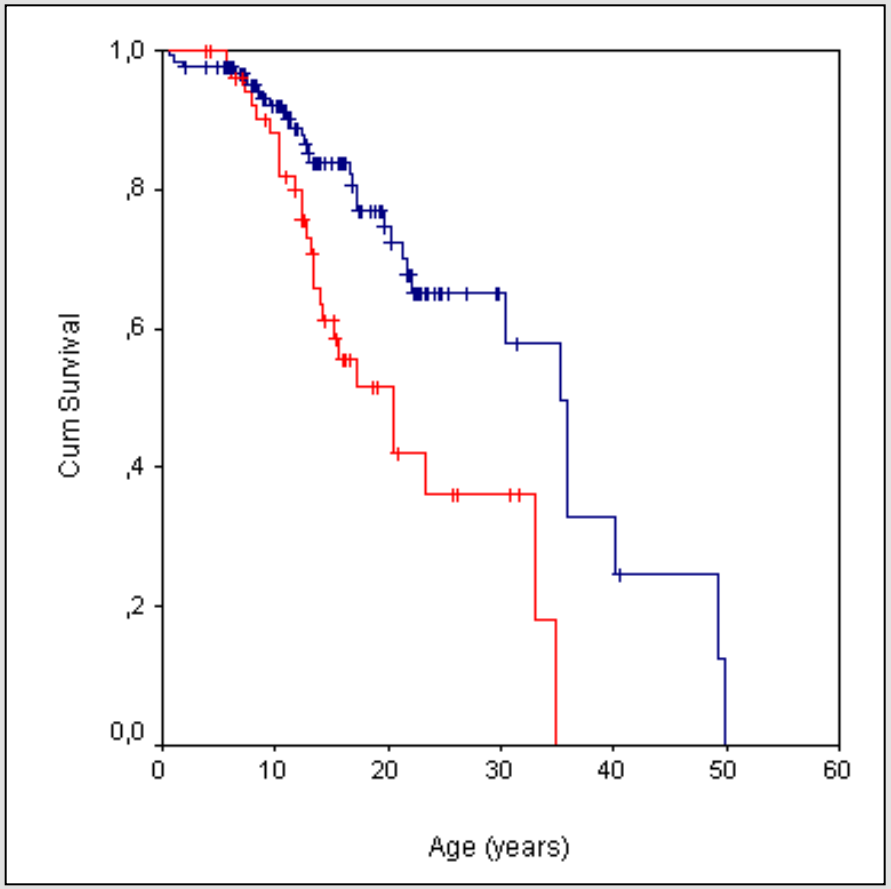
Stem Cell Transplantation

Wolfram Ebell

Pediatric Bone Marrow Transplant Service
Charité – Universitätsmedizin Berlin, Germany

Survival of FA patients

GEFA Registry (N = 233)



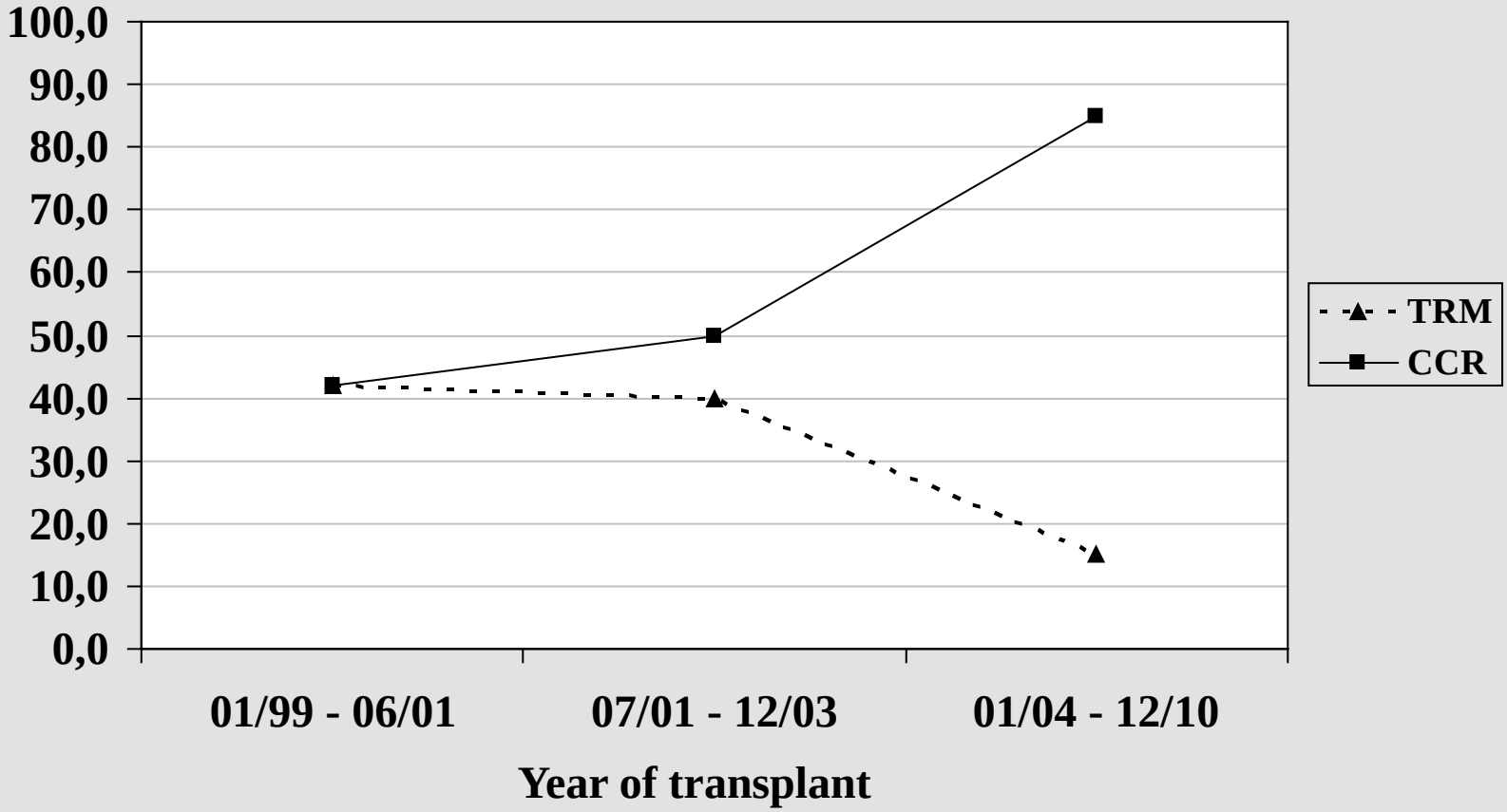
HSCT

No

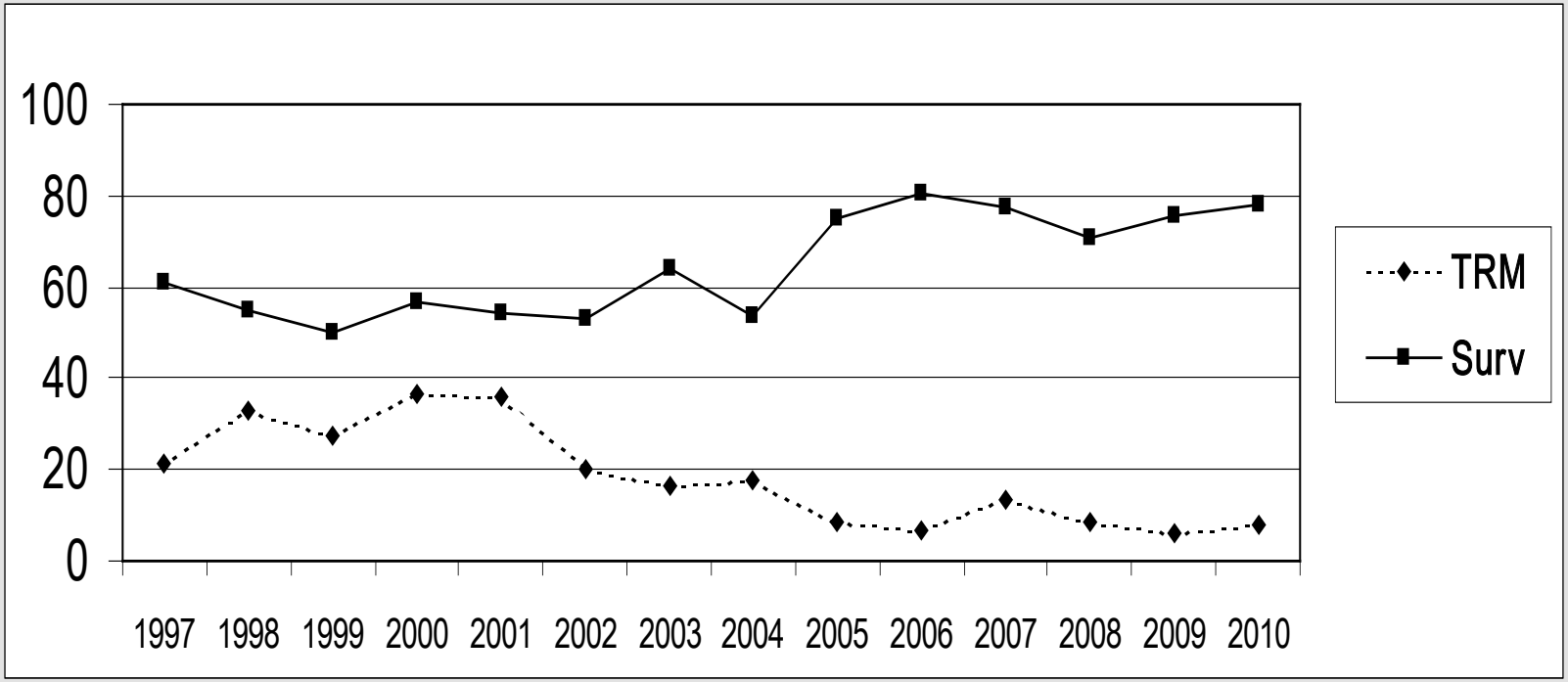
Yes

HSCT results (%)

FA patients 01/1999 – 12/2010 (Charité)

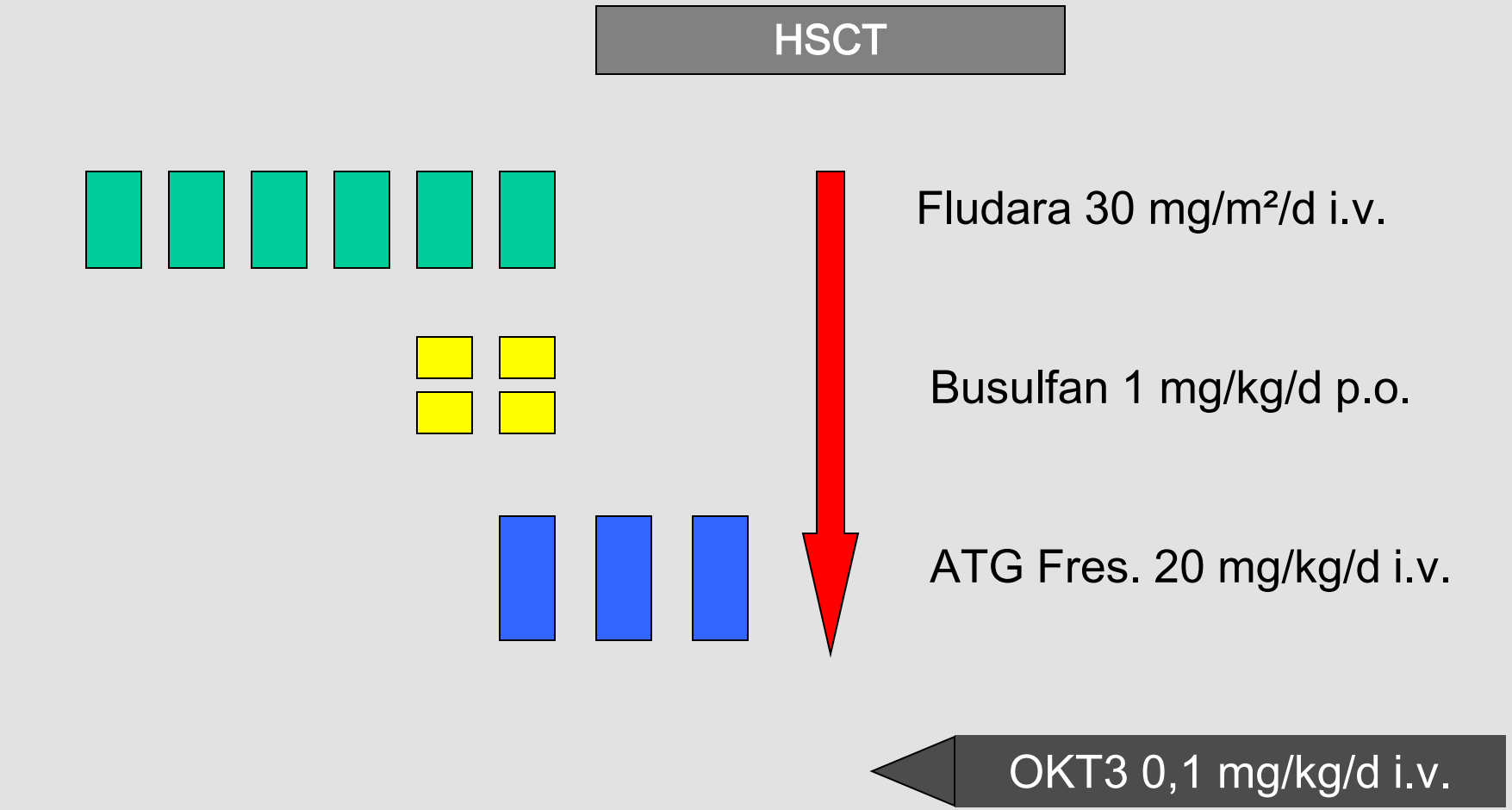


HSCT results (N=435)

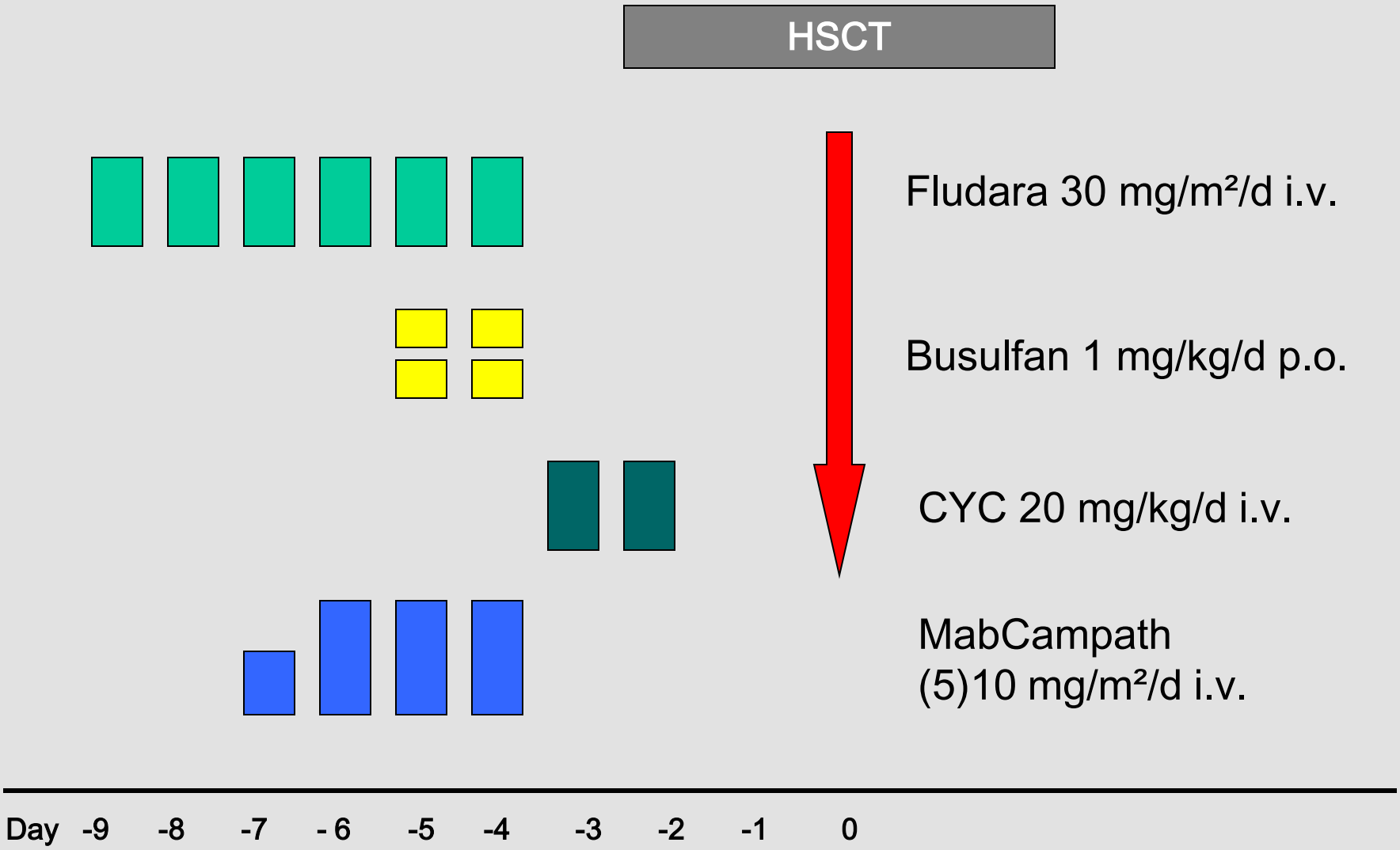


Transplant year

GEFA02 Protocol



GEFA03 Protocol



Patient characteristics

GEFA-protocols 05/2011

Total number of patients	27
Age	12 (2 – 25 years)
AA	12
MDS	13
AML	2
Cytogenet. aberration (3q+/-7)	15 (10/6)
Polytransfusion	17
Androgens	22
Liver adenomas	7
Mosaicism	2

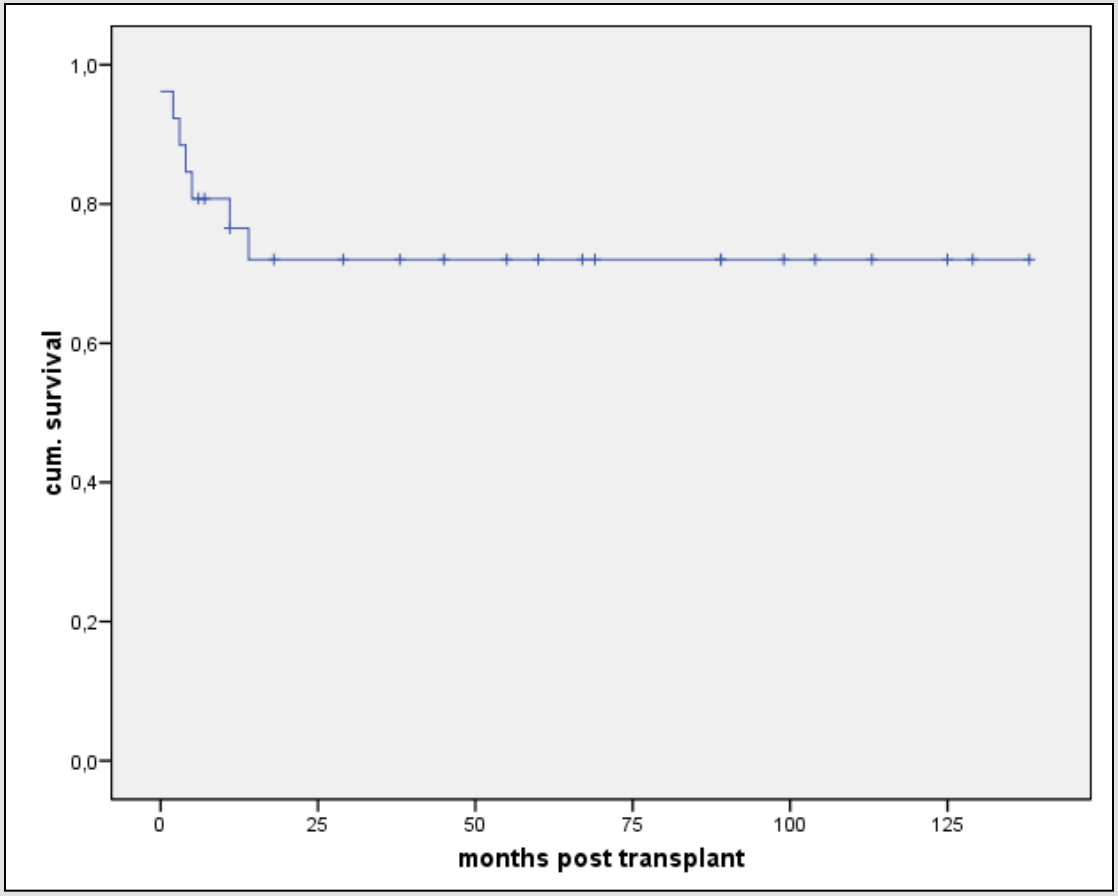
Transplant procedures

GEFA-protocols 05/2011

Total number of patients	27
GEFA02	18
GEFA03	9
(M)MFD (5/10, 8/10, 10/10)	4 (1, 1, 2)
(M)MUD (6/10, 7/10, 8/10, 09/10, 10/10)	23 (1, 1, 2, 2,17)
BM (T-Depletion)	16 (1)
PBSC (T-Depletion)	11 (4)

HSCT-results

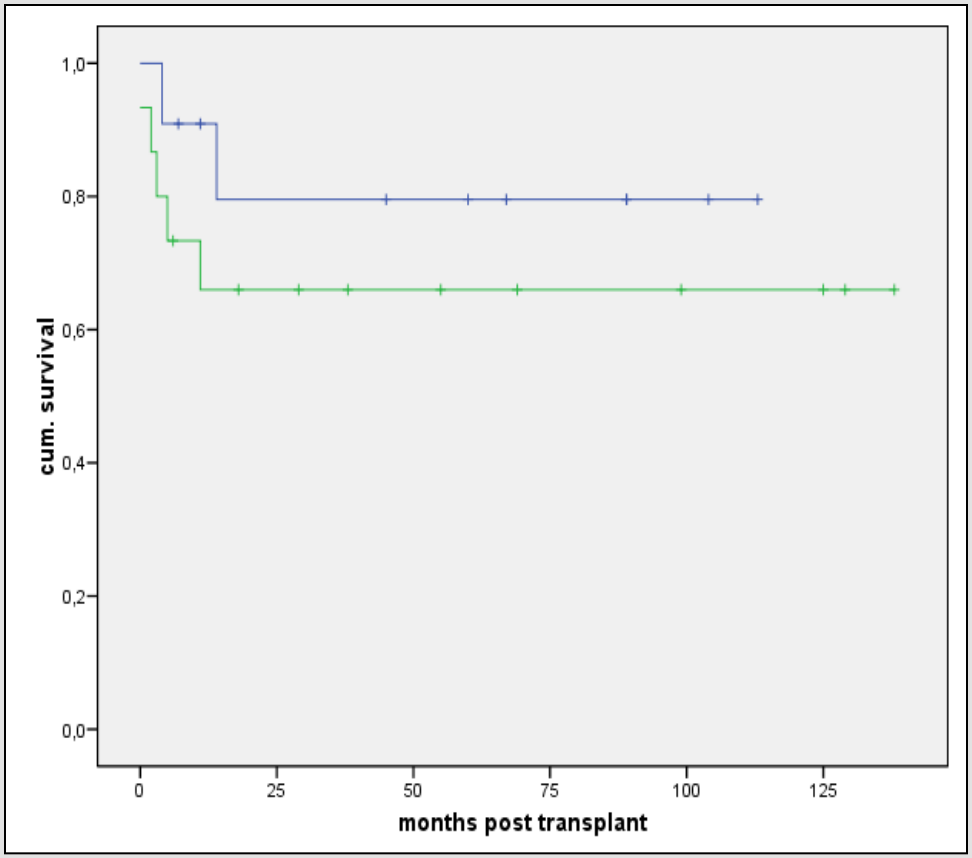
GEFA-protocols 05/2011 (N = 26)



pSurv 0.71 ± 0.09

HSCT-results

GEFA-protocols 05/2011 (N = 26)



pSurv

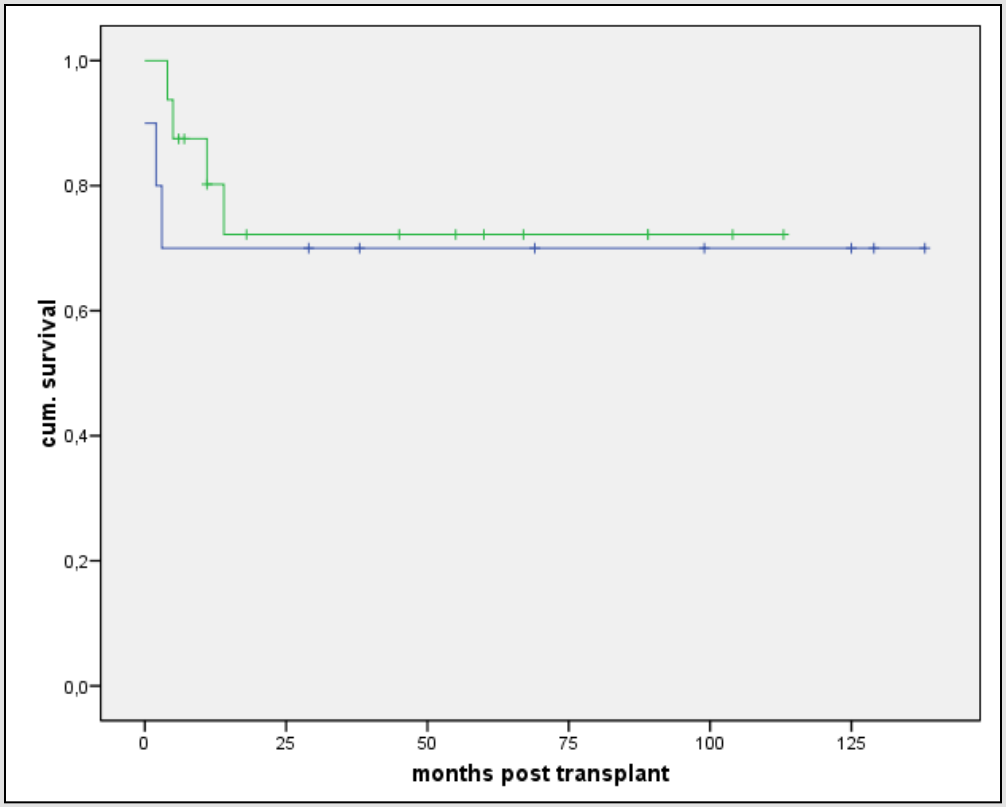
AA (n=11): 0.82 ± 0.12

MDS/AML (n=15): 0.66 ± 0.12

Log rank: n.s.

HSCT-results

GEFA-protocols 05/2011 (N = 26)



pSurv

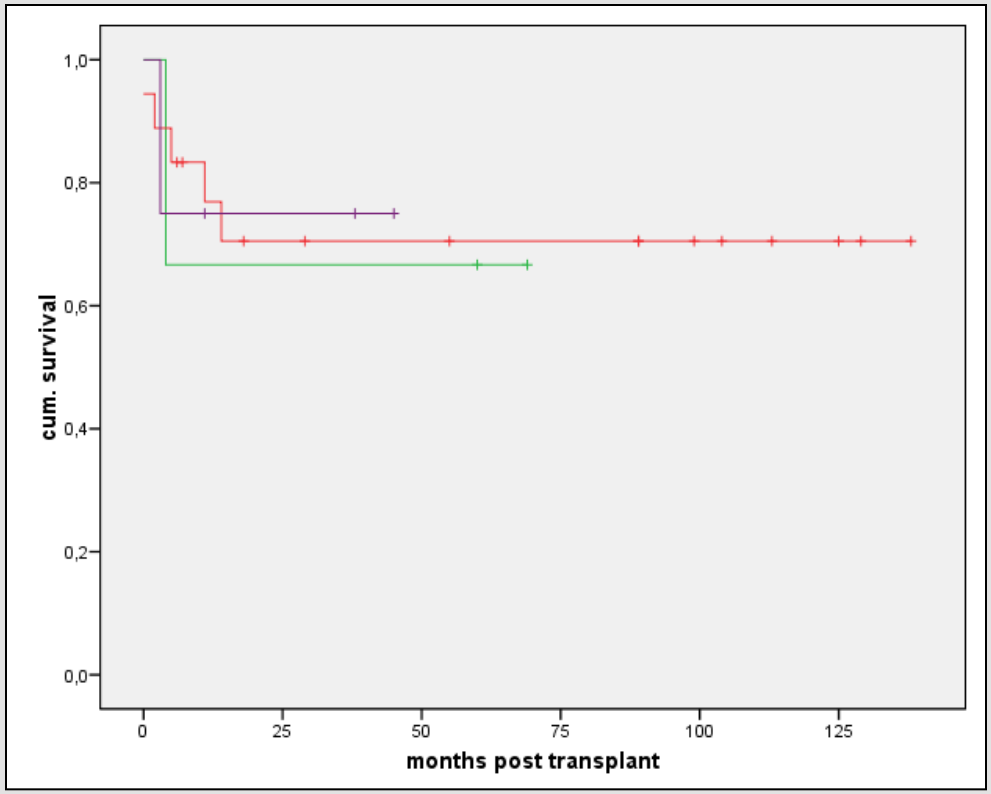
3q - (n=16): 0.74 ± 0.11

3q + (n=10): 0.70 ± 0.15

Log rank: n.s.

HSCT-results

GEFA-protocols 05/2011 (N = 25)



pSurv

MMUD (n=4): 0.75 ± 0.22

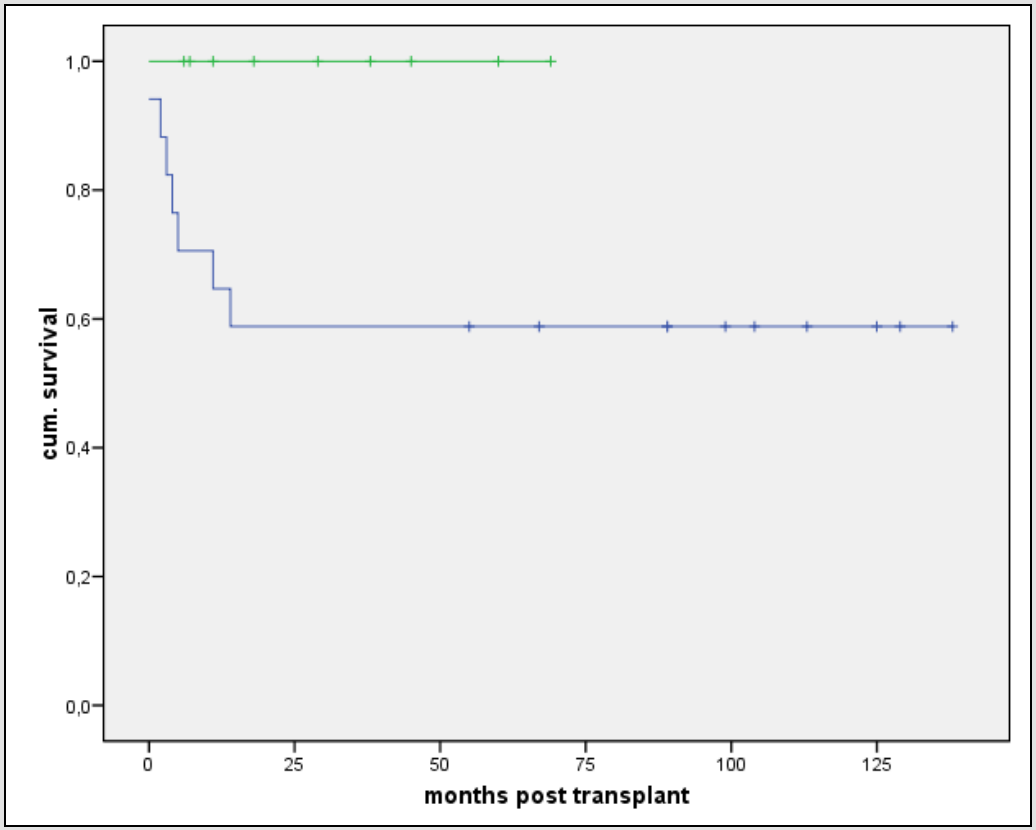
MUD (n=18): 0.72 ± 0.11

MMRD (n=3): 0.67 ± 0.27

Log rank: n.s.

HSCT-results

GEFA-protocols 05/2011 (N = 26)



pSurv

GEFA03 (n=9): 1.00 ± 0.10

GEFA02 (n=17): 0.61 ± 0.11

Log rank: 0.042

Patient characteristics

GEFA-protocols 05/2011

	GEFA02 (N=18)	GEFA03 (N=9)
Age	11 (2 – 25) years	13 (7 – 19) years
MDS/AML	56 %	56 %
Cytogenetic aberr.	61 %	44 %
3q+	39 %	33 %
Androgens	83 %	78 %
PBSC	44 %	33 %
< 9/10 HLA-identity	6 %	56 %
Survival	102 (55 – 138) months	29 (6 – 69) months

HSCT results

GEFA-protocols 05/2011

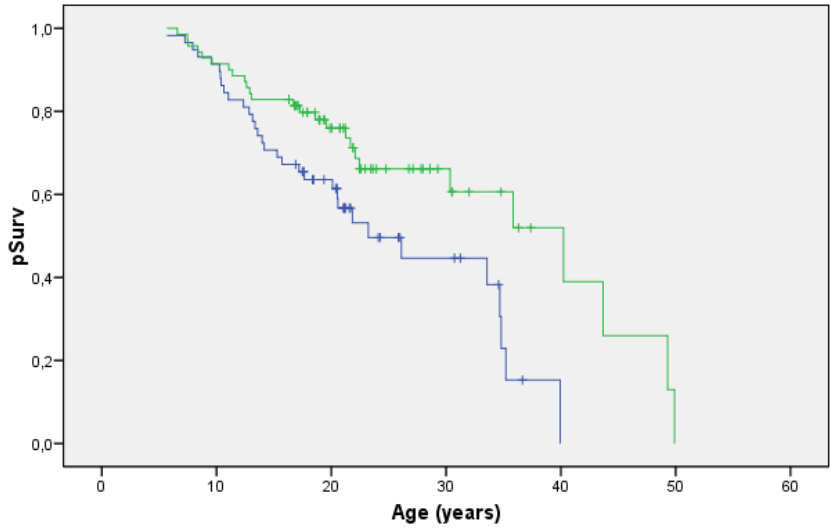
	GEFA02 (N=18)	GEFA03 (N=9)
Engraftment	18	9
Rejection / 2. transplant	2	0
Mixed chimerism / SC boost	3	0
Relapse / LD-CT + SC boost	0	1
SCC	1	0
aGVHD II / >II	3 / 0	0 / 0
cGVHD I / II	5 / 0	1 / 0
Cause of death	AML 1, SCC 1, virus 6	0

Survival of FA patients

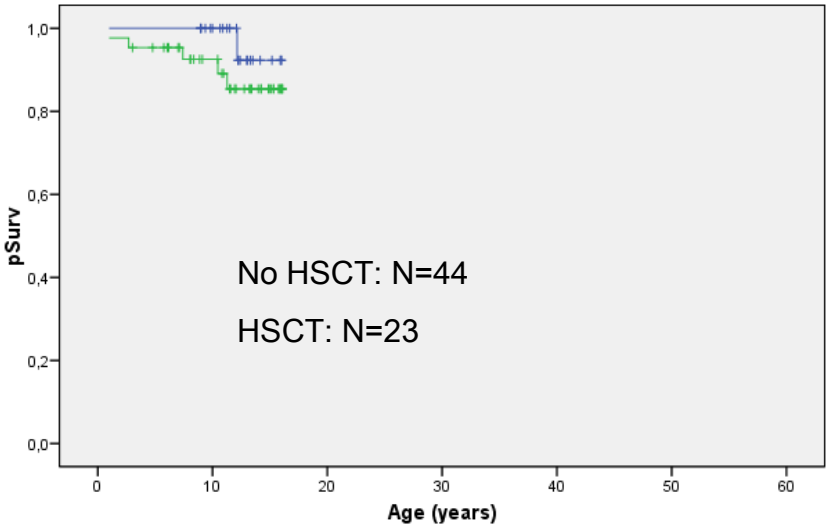
GEFA Registry (N = 233)

HSCT: No Yes

Born 1951 - 1994



Born 1995 - 2008



Summary (1)

- ✓ Alternative donor transplants are further improving in FA patients like in other diseases
- ✓ This can be achieved with fludarabine based non-irradiation protocols even in patients with clonal disease and/or mismatched donors
- ✓ Complete cell line specific donor chimerism some times requires several months
- ✓ The GEFA 03 protocol seems to offer a more stable engraftment with similar toxicity and perhaps less viral complications

Summary (2)

- ✓ FA patients with or without 3q+ aberrations have comparable transplant results
- ✓ Therefore, an early identification of this aberration might be a crucial indicator for an alternative donor transplant
- ✓ It still remains open which type and dose of alcylating agents as well as T-cell antibodies are the best choice, especially in respect to late effects (e.g. tumor risk)

Summary (3)

- ✓ In case of graft failure or relapse a mild chemotherapy and stem cell boost are sufficient salvage measures in most instances
- ✓ In individual patients significant modifications are necessary because of critical organ dysfunctions / malformations
- ✓ Probably also for FA there will be no difference any more between MUD and MRD in the future
- ✓ Whether this is also true for young adults with FA remains an open question
- ✓ There is no good solution for the rare but very severe complementation groups

Pediatric Bone Marrow Transplant Service

Charité Berlin

Clonal aberrations in FA patients: chromosomes involved