Emopatie non maligne e trapianto:

STANDARD ATTUALI E PROSPETTIVE FUTURE

Persistent mixed chimerism after HSCT for Aplastic Anemia: a case report

Napoli 24.01.2017

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Diagnosis

Li-Ma, 22 aa, ♂

APR: Ndp

APP: Feb 2015: fever, flu-like symptoms

02/MAR/2015: WBC 2680/mmc (ANC500/mmc)

Hb: 11,4 g/dl, RET: 0,37% (10.730/mmc)

PLT: 9000/mmc

Prednisone

Supportive therapy

23/MAR/2015: WBC 6630/mmc (ANC1900/mmc), **Hb ↓, PLT ↓, fever**

24/MAR/2015:

BOM → Hypoplastic Marrow (20% cell.), no MDS changes, lymph ↑

Aplastic Anemia ?

Referral to Federico II Hematology department

07/APR/2015: Access to Fed-II Bone Marrow Failure Unit (Prof. AM Risitano)

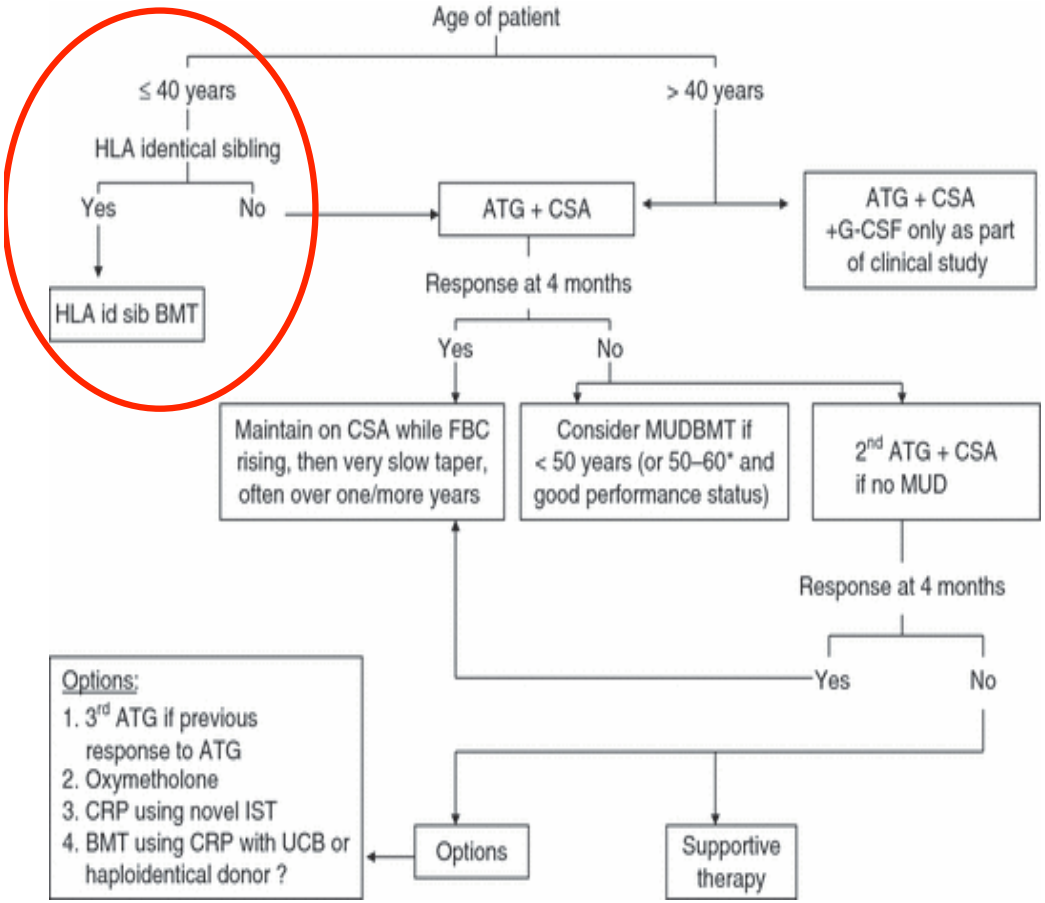
- ✓ Blood count: ANC 1760/mmc, PLT 11000/mmc, RET 16.500/mmc
- ✓ PNH clone on PB: **PMN 0.5%, Mo 1%**
- ✓ BOM revision: decreased per-age cellularity confirmed **(<20%)**
- ✓ DEB test on PB: Negative (+ carefoul family history ex.)

- ✓ Routine lab-clinical investigations, including Chest X-rays and Abdomen ultrasound

bjh guideline

Guidelines for the diagnosis and management of aplastic anaemia

Judith C. W. Marsh,[1] Sarah E. Ball,[2] Jamie Cavenagh,[3] Phil Darbyshire,[4] Inderjeet Dokal,[5] Edward C. Gordon-Smith,[1]

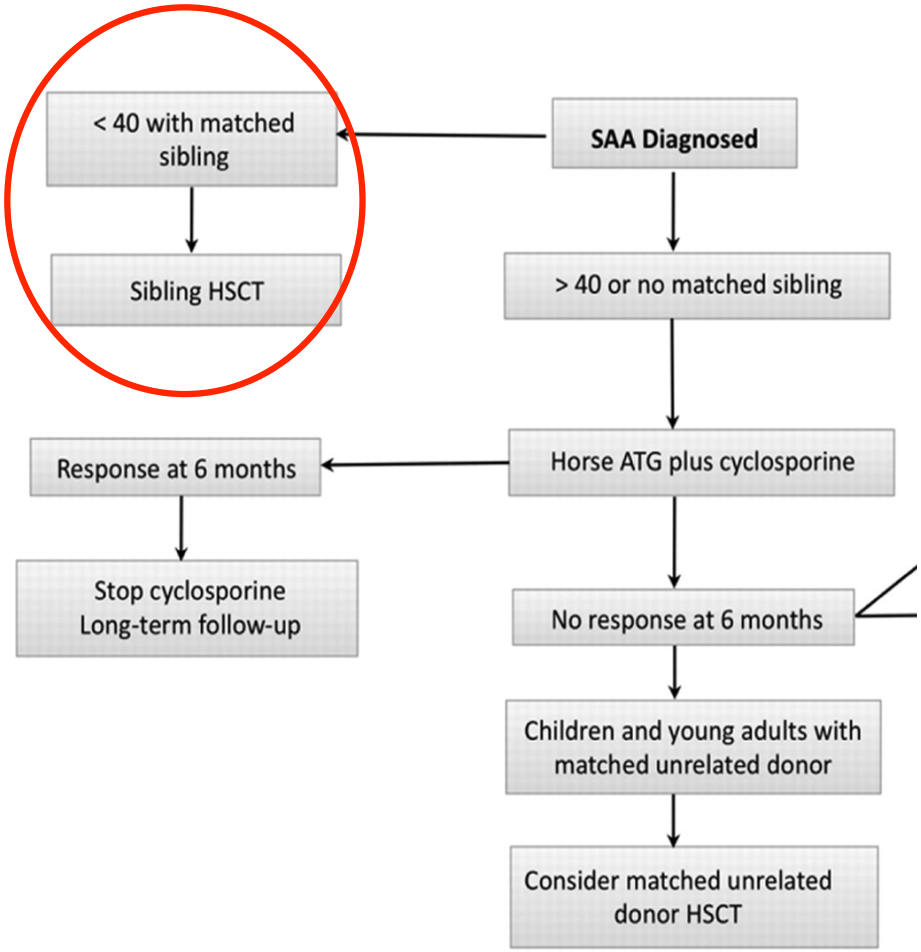


British Journal of Haematology
Volume 147, Issue 1, pages 43-70, 10 AUG 2009

How I treat acquired aplastic anemia

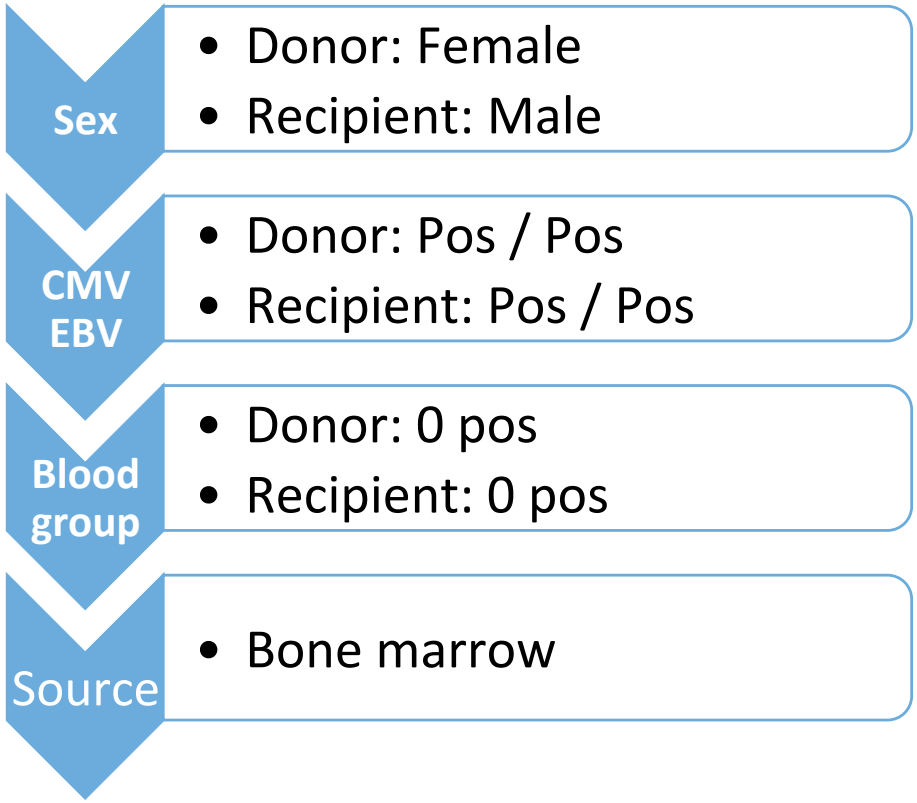
Phillip Scheinberg[1] and Neal S. Young[1]

[1]Hematology Branch, National Heart, Lung, and Blood Institute, Bethesda, MD



Phillip Scheinberg, and Neal S. Young
Blood 2012;120:1185-1196

First line treatment: HSCT from HLA-matched sib-donor



Conditioning and post-HSCT IST regimen selected

Cyclophosphamyde: 50 mg/kg, dd -6 → -3

Alemtuzumab: 15 mg, dd -6 → -3

CSA: 3 mg/kg from dd-1

HSCT outcome – day +30

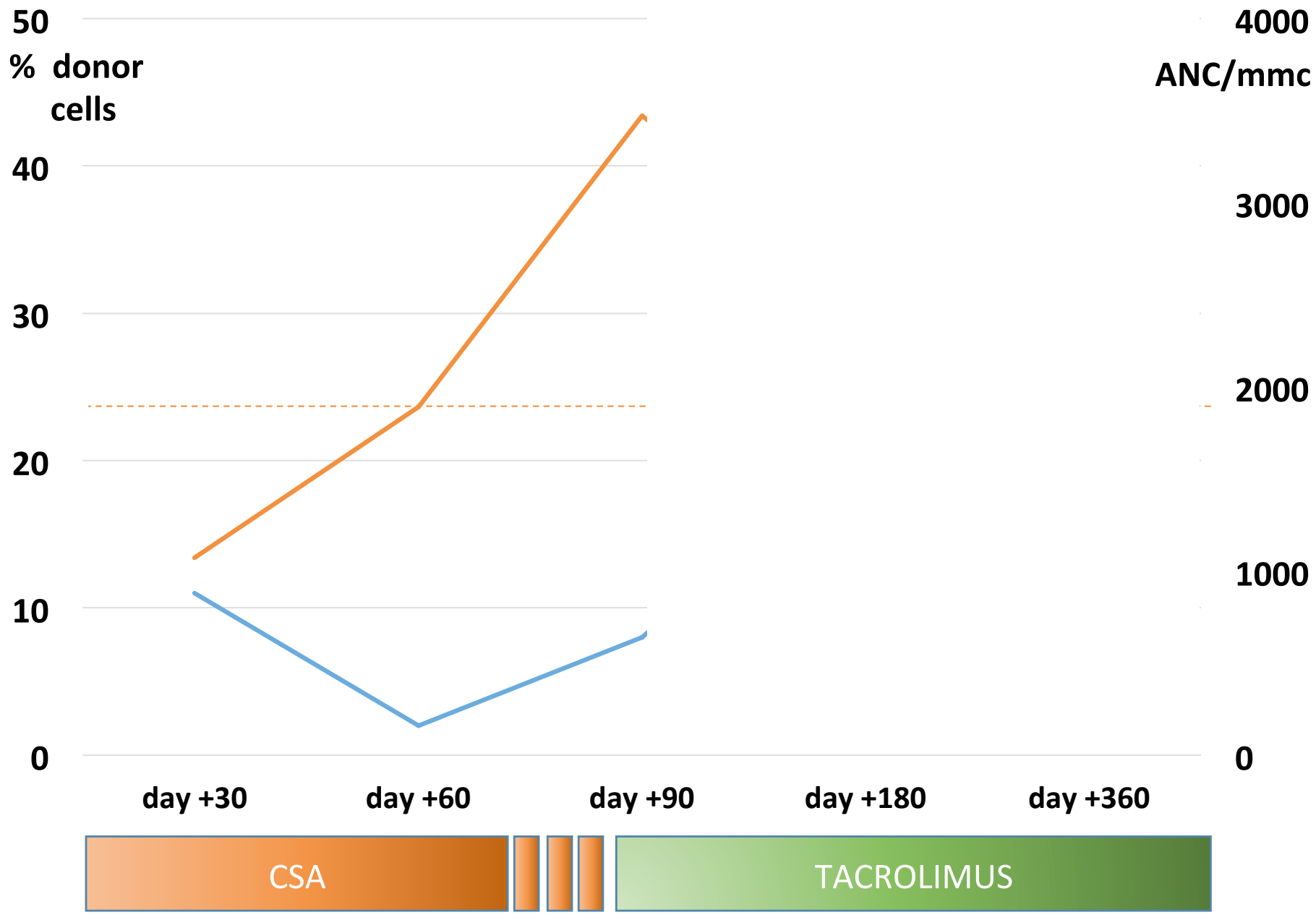
08/MAY/2015: starts conditioning regimen

15/MAY/2015: stem cell infusion (TNC: 1,46x10^8/kg ; CD34+: 1,35x10^6/kg)

- ✓ ANC>500/mmc d+18
- ✓ PLT>20.000/mmc d+27
- ✓ Minimal trasfusional support (6 ED + 2 PLT-POOL)
- ✓ No fever (d+27 CMV reactivation – no treatment needed)
- ✓ No symptoms/sign of Acute GvHD

11/JUN/15: discharged on d+28

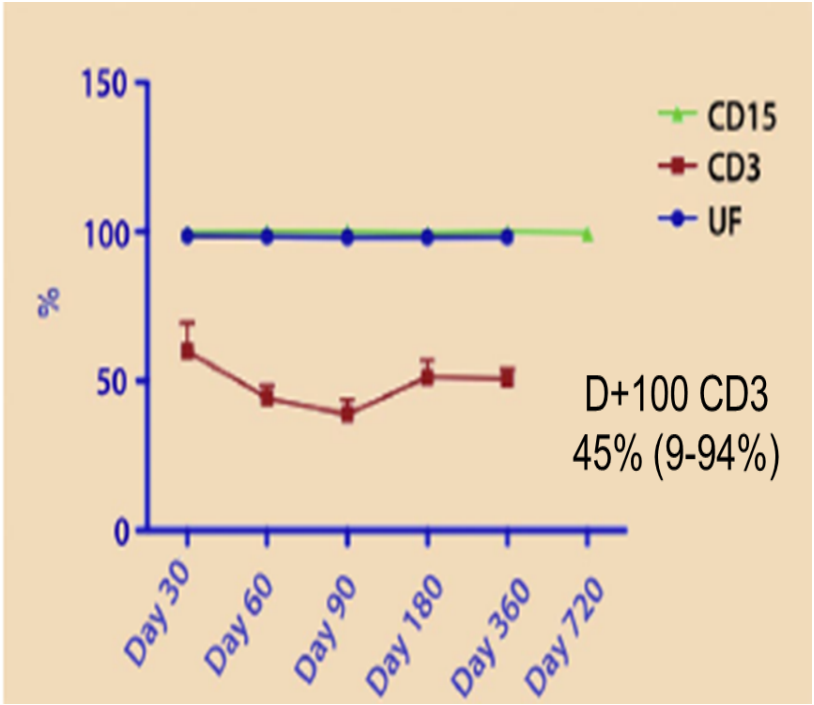
HSCT outcome and chimerism trend: day +30 → +365



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

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



Acute GVHD
13.5% (16.5% CI at 1yr)

Chronic GVHD
4% (7% CI at 1yr)

Graft failure
6 (12%), 3 primary, 3 secondary
9.5% MSD, 14.5% UD

Bone Marrow Transplantation (2014) 49, 42–48

www.nature.com/bmt

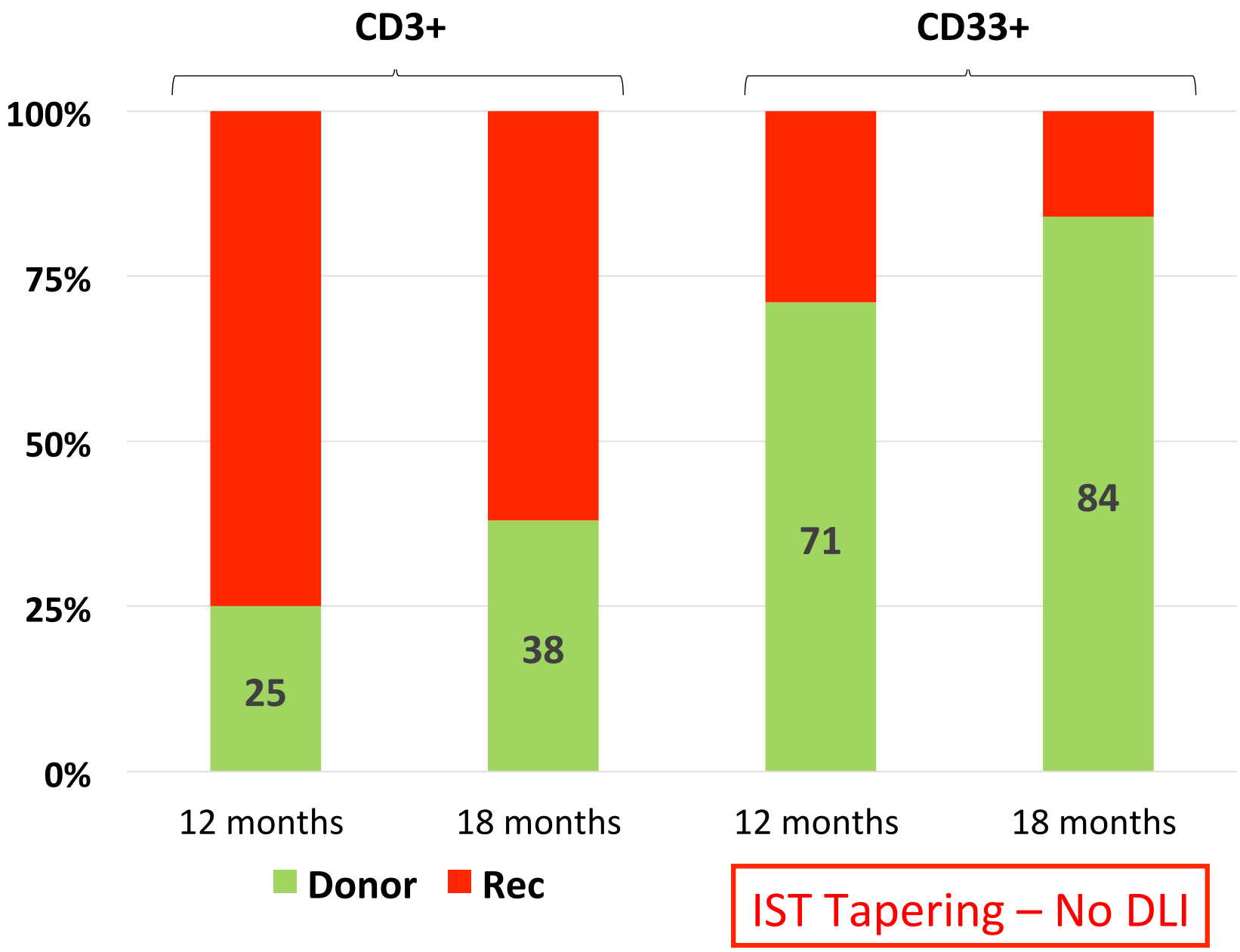
ORIGINAL ARTICLE

Retrospective study of alemtuzumab vs ATG-based conditioning without irradiation for unrelated and matched sibling donor transplants in acquired severe aplastic anemia: a study from the British Society for Blood and Marrow Transplantation

JC Marsh[1], RM Pearce[2], MBC Koh[3], Z Lim[4], A Pagliuca[1], GJ Mufti[1], J Perry[2], JA Snowden[5,6], AJ Vora[7], RT Wynn[8], N Russell[9], B Gibson[10], M Gilleece[11], D Milligan[12], P Veys[13], S Samarasinghe[14], M McMullin[15], K Kirkland[2] and G Cook[11] on behalf of the British Society for Blood and Marrow Transplantation (BSBMT) Clinical Trials Committee (CTCR 09-03)

	Alemtuzumab	*ATG*
Median age (range)	18 (1–67)	21 (2–57)
<18 years	50 (50%)	17 (31%)
⩾18 years	50 (50%)	38 (69%)
Donor		
Matched sibling	44 (43%)	43 (78%)
MUD	55 (55%)	7 (13%)
Mismatched UD/other related	1 (1%)	5 (9%)
Conditioning		
CY 200 mg/kg	32 (32%)	43 (78%)
Fludarabine-based	60 (60%)	9 (16%)
TBI	8 (8%)	3 (5%)
Neutrophil recovery (days)	19 (10–89)	21 (12–34)
Platelet recovery (days)	20 (0–275)	21 (3–47)
Chimerism at 100 days		
Complete donor	44 (58%)	21 (66%)
Mixed	30 (39%)	10 (31%)
None	2 (3%)	1 (3%)
Chimerism at last FU		
Complete donor	37 (54%)	20 (71%)
Mixed	30 (43%)	8 (29%)
None	2 (3%)	0 (0%)

Chimerism trend: 12→ 18 months



HSCT outcome – 9 Jan 2017, last update

No signs/symptoms of GvHD

No clinically significant infectious episodes

CMV reactivated, but not treated

Off immune-suppressive therapy?

09/Jan/2017: WBC 2.630/mmc (ANC 1.010/mmc), PLT 119.000/mmc, Hb: 13,7 g/dl

Chimerism level: waiting for new results

Restarted on CSA and MMF

Conclusions

Alemtuzumab-based HSCT good platform for AA treatment

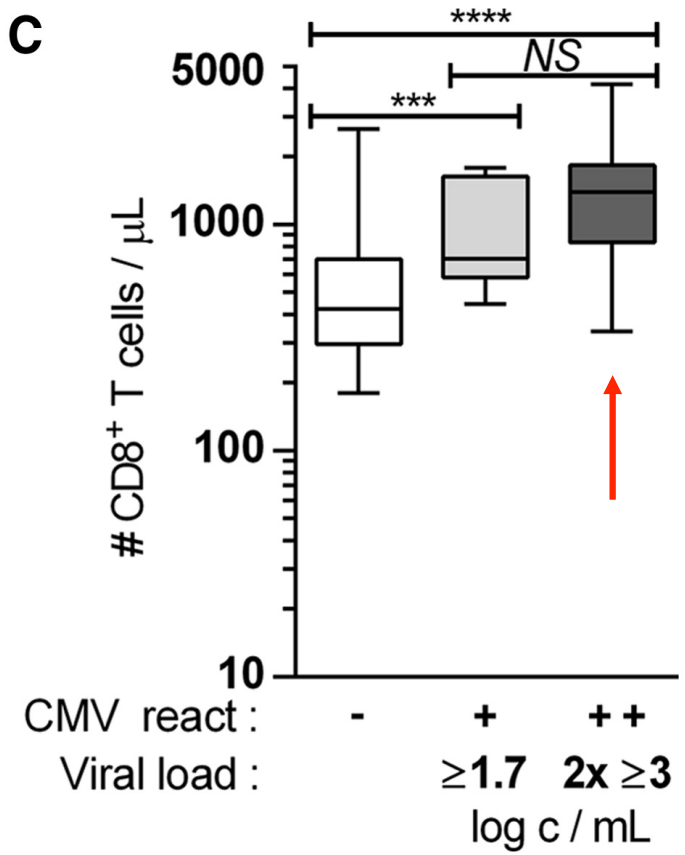
Chimerism patterns different from ATG-based HSCT

Persistently low level of chimerism not predictive for graft failure (?)

Persistently mixed chimerism status = GvHD protection (?)

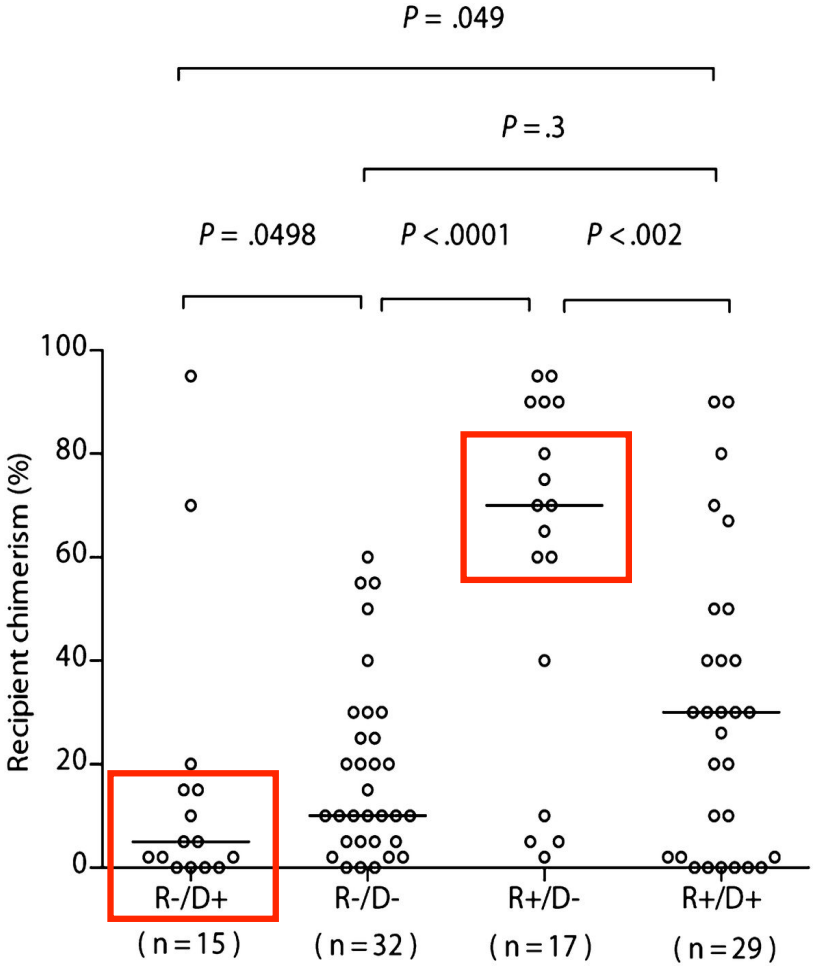
Early Cytomegalovirus Reactivation Leaves a Specific and Dynamic Imprint on the Reconstituting T Cell Compartment Long-Term after Hematopoietic Stem Cell Transplantation

Gertjan Lugthart [1,*], Monique M. van Ostaijen-ten Dam [1], Cornelia M. Jol - van der Zijde [1], Tessa C. van Holten [1],



CMV promotes recipient T-cell immunity following reduced-intensity T-cell–depleted HSCT, significantly modulating chimerism status

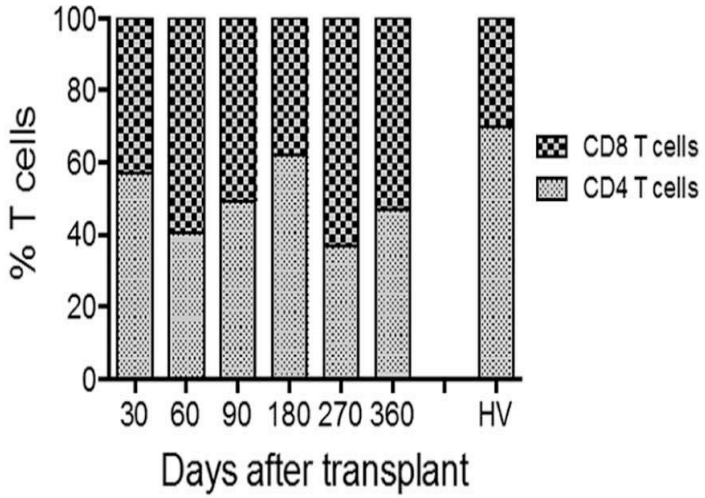
Rob S. Sellar,[1,2] Frederick Arce Vargas,[1] Jake Y. Henry,[1] Stephanie Verfuerth,[3] Sarah Charrot,[2] Brendan Beaton,[3] Ronjon Chakraverty,[3] Sergio A. Quezada,[1] Stephen Mackinnon,[3] Kirsty J. Thomson,[2] and Karl S. Peggs[1,2]



ASBMT
American Society for Blood and Marrow Transplantation

Mixed T Cell Chimerism After Allogeneic Hematopoietic Stem Cell Transplantation for Severe Aplastic Anemia Using an Alemtuzumab-Containing Regimen Is Shaped by Persistence of Recipient CD8 T Cells

Francesco Grimaldi [1,2], Victoria Potter [1], Pilar Perez-Abellan [3], John P. Veluchamy [3], Muhammad Atif [3], Rosemary Grain [3], Monica Sen [3], Steven Best [1], Nicholas Lea [1], Carmel Rice [1], Antonio Pagliuca [1], Ghulam J. Mufti [1,3], Judith C. W. Marsh [1,3,*], Linda D. Barber [3,†]



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