1. Relapses after allo. HCT
2. ABMT Toxicity & Risk Score
3. SAA
4. PRESIDENT: Hal E. Broxmeyer & the CBT Story
5. Plenary Session: New Concepts! New Indications!
6. New Cell Sources (beyond BM/PB/UCB)?
Allogeneic Hematopoietic Stem Cell Transplantation (HSCT): Interim-Analysis From the Acute Myeloid Leukemia (AML) or Myelodysplastic Syndromes (MDS) Relapsing After Allogeneic HSCT (SFGM-TC).

After allogeneic HSCT seems to be safe and shows significant anti-leukemic activity. Median overall survival (OS) and disease-free survival (DFS) were significantly longer in pts in first relapse (median follow-up 123 vs 30 days, p < 0.001) and pts with NHL or Hodgkin disease (70% vs 30% at 3 years, p = 0.01) versus other diagnoses. Multivariate analysis: diagnosis of NHL or Hodgkin disease (HR=0.33, 95%CI, 0.2-0.5), age (HR=0.89, 95%CI, 0.8-1.0) and sex (HR=0.84, 95%CI, 0.7-1.0) were associated with a significantly longer OS. Only age (HR=0.89, 95%CI, 0.8-1.0) and sex (HR=0.68, 95%CI, 0.5-0.9) were associated with a longer DFS. Conclusion: Aza + DLI is an effective salvage therapy for patients with active refractory/reapsed hematological diseases, especially in patients with lymphomas.
In the absence of an identical sibling ATG+CSA is the standard 1st line treatment?
LBA-4: A Randomized Trial of Horse Versus Rabbit Antithymocyte Globulin In Severe Acquired Aplastic Anemia
Ph Scheinberg, CO Wu, P Scheinberg, B Weinstein, D Nunez, EM Slouad, NS Young Hematology Branch, National Heart, Lung, and Blood Institute, NIH
Late-breaking Abstracts Session: Tuesday, 7:30 AM Hall D
Hematologic response rates at 6 months in evaluable patients
Horse ATG 37/54 (69%) vs Rabbit ATG 19/54 (35%)

Scores 1, 2, 3, 4... 6 months 0 1 2 3

Efficacy of Rabbit Anti-Thymocyte Globulin (ATG) Compared to Horse ATG In Severe Aplastic Anemia
Bone Marrow Failure: Poster II Sunday
M Afable, M Shaik, Y Sugimoto, M Clemente RV Tiu, SR. Mohan, N Bejanyan, P Elson, M Kalaycio, A Advani, R Sobecks, AE Lichtin, MA Sekeres, J Maciejewski
rATG: 22, hATG controls: 67
Response was similar for pts treated with rATG compared to hATG at:
3 months: 41% vs. 52% (p=.15)
6 months: 50% vs. 59% (p=.62)
12 months: 54% vs 59% (p=.66)

Comparison between Lymphoglobuline- and Thymoglobuline-based immunosuppressive therapy as first-line treatment for patients with Aplastic Anemia

1st IST course (131 pts) best response
OR: 58 % (Thymo: 57.8%; Lympho: 58.5%; p=NS)
PR: 33 % (Thymo: 38.9%; Lympho: 19.5%; p=NS)
CR: 25 % (Thymo: 18.9%; Lympho*: 39%; p=NS)

Oral presentation: 24 months

Given all this information
IS vs BMT
Life could be easy if we knew
Who will respond to IS?
Who will not suffer from severe GvHD?

High-dose cyclophosphamide for severe aplastic anemia: long-term follow-up
Biol Haematol Oncol 2010 115:2136

Question: Why not CBT? (HEB)
Stem Cell Potency

Totipotent Stem Cells: can construct a complete viable organism

Pluripotent Stem Cells: can differentiate in any cells derived from the three germ layers

Multipotent Stem Cells: can differentiate into more than 3 lineages within one germ layer

Unipotent cells: produce only one cell type, their own

Safety for Regenerative Medicine

Tumorigenicity:
Some of the genes that are transfected for iPS generation, like c-myc, are also known to act as proto-oncogenes.

One of the characteristics of pluripotent cells is spontaneously teratoma formation in vivo.

Chimeric mice produced from iPS cells show a high incidence of death from malignant cancer.

Viral transfection:
bears potential risks such as malignant transformation and immune responses to viral proteins.

CASE (Agarwal / Daley)
- newborn + severe anemia
- Vacul. RBC precursor
- Ringsiderobl.
- D.m.
- DNA diag. -> mtch. DNA mutation
- BM Fb. (MSC) culture (75% heteroplasmy = defect. mtch.)
- over 2-3 mo. Culture = LOSS OF HETEROPLASM (purged iPS)
- culture + hematop. CK -> virtually disease-free blood cells
- 2 more pt. (n=3) with heteroplasmy <75%
- VISION: autologous iPSC therapy by selection culture


Vanderson Rocha 1*, Myriam Labopin, MD 2*, Annalisa Ruggeri, MD 1*, Marina Podestà 3*, Dolores Caballero 4*, Francesca Bonifazi, MD 5*, Rovira Montserrat 6*, Andrea Gallamini, MD 7, Franca Fagioli, MD 8*, Gérard Socié, MD 9, E. Nikiforakis 10*, Mauricette Michallet 11, Eric Deconinck 12*, Mohamad Mohty 13, Andrea Bacigalupo, MD 3, Eliane Department, CHU de Nantes, Nantes, France

The limited hematopoietic progenitors in UCB grafts and their homing after IV injection, have prompted … delivering CB grafts directly into the bone marrow (BM) space (IBCBT) or to use double cord blood transplantation (dUCBT) to improve engraftment. To evaluate the impact of iCBT - transplantation of BM cells (IBCBT) … 0.03). Median number of apheresis (after thawing) was 2.5 x 10^7/kg in IBCBT (p<0.01). 74% of CMV sero-converters were CMV negative in 23/33 donors (IBCBT) and 64% in 31/48 donors (dUCBT).

@ day 30, CI of ANC >500 was 83% after IBCBT and 63% after dUCBT (p=0.001)

Unadjusted 2 y-DFS estimation was 47% after IBCBT and 37% after dUCBT (p=NS).

CONCLUSION: both strategies have extended the use of CB transplants to adults in need of cord blood transplantation. Therefore, IBCBT is an option to transplant adult patients with single CB units after myeloablative conditioning regimen and may impact the total costs of cord blood transplantation. Based on these results, intra-bone technique may disclose new transplant potentialities also with other HSC sources.
Outcomes of Second Unrelated Cord Blood Transplant for Relapse After First Allogeneic Transplant in Adult Patients with Progressive Acute Myeloid Leukemia/Myelodysplastic Syndrome

Sachi Tainosho, MD, PhD; Kayoko Masuda, MD, PhD; Aya Nishida, MD, PhD; Nobuo Shimosaka, MD, PhD; Kazuya Ishiwata, MD, PhD; Masanori Tsuji, MD, PhD; Hisashi Yamamoto, MD, PhD; Naoyuki Uchida, MD, PhD; Atsushi Wake, MD, PhD; Shuichi Taniguchi, MD, PhD

Tokyo, Japan

Retrospective analysis of 2nd allo-HSCT using UCB for 34 adult patients with AML/MDS relapsed after 1st HSCT. 130 adult patients with AML/MDS (21/13) underwent 1st HSCT… 53 relapsed, 34 = 2nd Tx with UCB (19/4 did not receive 2nd Tx – severe organ dysfunction or uncontrolled active infection or CR by donor lymphocyte infusion). The median age at 2nd UCBT was 54 years (18-69) and interval between 1st allo-HSCT and 2nd UCBT was 9 months (1-48). All patients at 2nd UCBT were in progressive disease – received a single cord blood unit with median TNC/CD34 cell dose of 2.8×10^7/kg (range, 1.4-4.8) and 0.7×10^5/kg (range, 0.2-2.2), respectively. HLA disparities were 3/6 match (n=4), 4/6 (n=25), 5/6 (n=4) and 6/6 (n=1). Conditioning regimen consisted of fludarabine and alkylating agent. Graft-versus-host disease (GVHD) prophylaxis consisted of tacrolimus (Tac) alone in 15, Tac plus mycophenolate mofetil in 11, and cyclosporine alone in 8. 10 patients died by day 28 (PD=5; TRM=5). 24 patients survived > 28 days, aGVHD developed in 14, cGVHD in 4.

Estimated 3-year OS, TRM and relapse mortality rate were 16%, 32%, and 52%. Univariate analysis: worsened survival if early relapse < 100 days after 1st allo-HSCT (0 vs 21%; P=0.01). Eighteen of 20 patients who did not undergo 2nd UCBT died of progressive disease or multiple organ failure.

Conclusion: 3 year-OS of 16% with 2nd UCBT following relapsed AML/MDS comparable with 2nd BMT or PBSC.

Considering that all patients in the study were in non-remission and in relatively higher age (median age 54 years), 2nd UCBT following relapse of AML/MDS could be a viable therapeutic option.