

(primarily pre-donation) but better mental health. There was no main effect difference by data collection time point and no age by time interaction for physical or mental health. Despite having somewhat poorer overall general pre-donation health, older RD experience similar – and in some domains better—donation-related HRQoL compared to younger RD. This is a reassuring finding that supports the use of older family members as donors and will further inform the counseling and consent of older RD.

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### Results of Allogeneic Double Umbilical Cord Blood Transplantation for Relapsed and Refractory Hodgkin Lymphoma

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**Introduction:** Allogeneic hematopoietic cell transplantation is effective in patients (pts) with high-risk

**Table**

| Characteristic, N = 27                                    | n (%) unless stated    |
|---|------------------------|
| Male gender   | 16 (59)                |
| Age at dUCBT, median (range)                              | 29 (17-61)             |
| Prior autologous transplant                               | 25 (92.5)              |
| Response prior to dUCBT                                   |                        |
| Complete Remission  | 6 (22.2)               |
| Partial Remission   | 9 (33.3)               |
| Stable Disease  | 5 (18.5)               |
| Progressive Disease                                       | 7 (26)                 |
| Conditioning Regimen                                      |                        |
| Fludarabine/low-dose cyclophosphamide/<br>TBI 2Gy +/- ATG | 10 (37)                |
| Fludarabine/Clofarabine/Busulfan/ATG/<br>TBI 2 Gy         | 3 (11)                 |
| Fludarabine/Melphalan/ATG                                 | 2 (7.5)                |
| Melphalan/Thiotepa/Fludarabine/ATG                        | 12 (44.5)              |
| Total Nucleated Cell Dose (x10 <sup>9</sup> /kg)          | 0.44 (range 0.12-5.94) |
| HLA match   |                        |
| 4/6, 4/6  | 15 (55.6)              |
| 4/6, 5/6  | 6 (22.2)               |
| 5/6, 5/6  | 5 (18.5)               |
| 6/6, 6/6  | 1 (3.7)                |

lymphoid malignancies including Hodgkin lymphoma (HL). We studied 27 pts who received double umbilical cord blood transplant (dUCBT) at The UT M.D. Anderson Cancer Center or The Royal Melbourne Hospital, Australia for relapsed/refractory HL.

**Patients and Methods:** Median number of prior treatments was 4 (range 2-6); 25 of 27 had had prior autologous transplant. 45% did not achieve at least partial response to their most recent prior therapy and 26% had progressive disease. Pts were treated consecutively between Aug 2003 and May 2014. All pts received dUCBT from 4/6-6/6 matched cord blood units. Graft versus host disease (GVHD) prophylaxis was tacrolimus or cyclosporine plus low dose methotrexate or mycophenolate mofetil. Pts were treated on ex vivo expansion studies using liquid culture media (N=8), mesenchymal stromal cells (N=3) or fucosylation (N=3) as available.

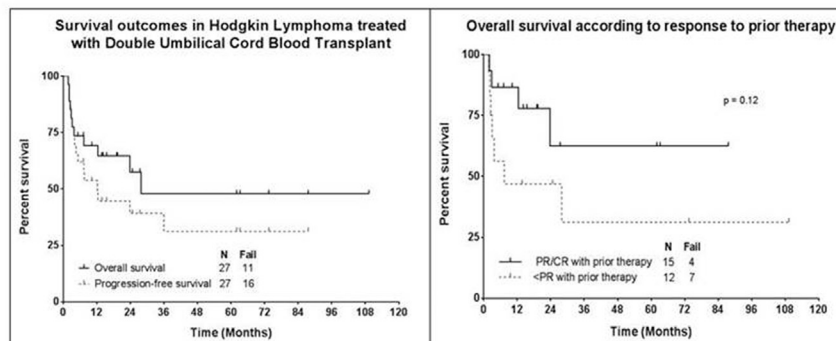
**Results:** Pt and transplant characteristics are described in **Table 1**. All pts engrafted. Median time to neutrophil recovery (ANC > 500/mm<sup>3</sup>) was 17 days (range: 5-38). Median follow-up after transplant was 14 months. Cumulative incidences of grade II acute GVHD and extensive chronic GVHD were 33.5% (95% CI 18.8-52.4) and 40.5% (24.7-59.6), respectively. No pt developed grade III-IV acute GVHD. Sixteen of 27 pts achieved complete remission (CR) after alloHCT; 7 had progressive disease at a median time of 7.4 months post-transplant (range 4.1-36.0). At the time of last follow up 16 of 27 pts were alive. Relapse contributed to death in 3 pts. The 5-year cumulative incidence of non-relapse mortality (NRM) was 37.9% (95% CI: 20.9-59.0). Five year probabilities of progression free-survival (PFS), and overall survival (OS) were 31.3 (95% CI: 15.0-54.0) and 47.9 (95% CI: 26.2-70.5), respectively (**Figure**). Small numbers limited the ability to define prognostic factors; however there was a trend toward inferior survival in pts achieving less than PR to their most recent prior treatment (p=0.12).

**Conclusions:** dUCBT is effective for patients with advanced HL. Relapse rate was low and approximately 30% of pts achieve long-term disease-free survival, including pts with chemorefractory disease prior to dUCBT.

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### Acceleration of Umbilical Cord Blood (UCB) Stem Engraftment: Results of a Phase I Clinical Trial with Stemregenin-1 (SR1) Expansion Culture

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**Figure.** Left: PFS and overall survival for all patients. Right: Overall survival according to therapeutic response (PR/CR vs <PR) prior to transplantation.

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UCB has been substantially limited by the low finite number of CD34+ cells, resulting in slow hematopoietic recovery and poor engraftment. SR1 is an aryl hydrocarbon receptor antagonist that enables CD34 cell proliferation in the presence of SCF, Flt-3L, IL-6 and TPO. Therefore, we tested the safety and efficacy SR1-expanded UCB (referred to as 'HSC835'). Nineteen patients (pts) with high-risk hematologic malignancy have been treated with HSC835 after myeloablative conditioning (cyclophosphamide 120 mg/kg, fludarabine 75 mg/m<sup>2</sup> and TBI 1320 cGy) with CsA and MMF post-transplant immune suppression. The first 17 received an unmanipulated second 'back-up' UCB unit. SR-1 expansion culture yielded a median of 1,440 × 10<sup>6</sup> CD34+ cells (range, 140.2–6361.9), a 328-fold (range, 65.9–844.0) expansion of CD34+ cells, for a median infused dose of 12.3 × 10<sup>6</sup> CD34+ cells/kg (2.3–48.5). As shown (Figure), all patients engrafted with the HSC835 unit predominating in 11/17 at a median of 11 days for neutrophils (6–23). As expected, unit predominance was determined by graft-graft immune reactions, as evidenced by the presence of interferon-γ producing T cells directed against the losing graft. Chimerism in HSC835 engrafted patients was stable long term with no episode of late graft failure. Compared to 111 identically treated DUCB transplant historical controls without

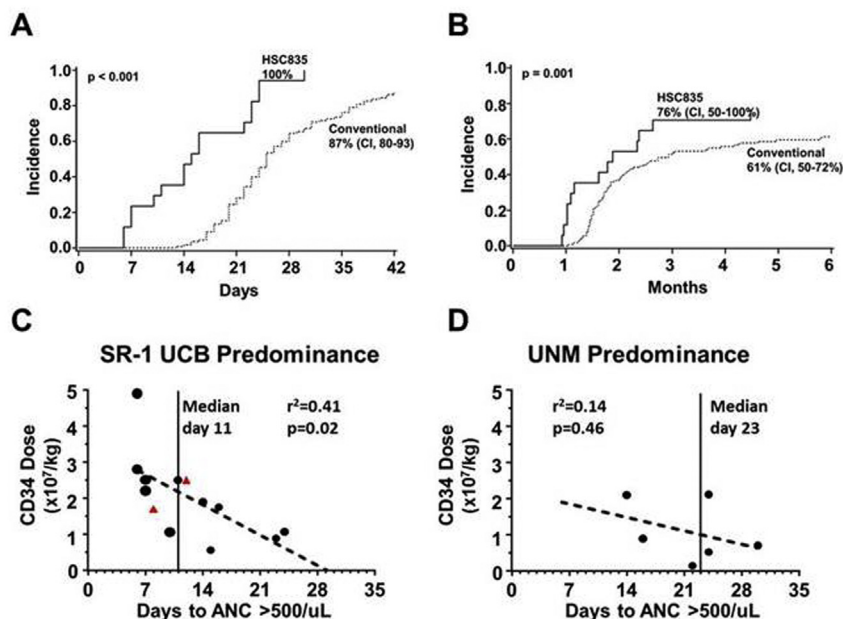
expanded cells (conventional arm), neutrophil and platelet recovery was remarkably shortened in HSC835 recipients (p<0.001 and p=0.001, respectively). Based on these data, a second trial with HSC835 as a stand-alone graft was initiated. In two patients, receiving 25 and 18 × 10<sup>6</sup> CD34/kg, neutrophil recovery was rapid (days 12 and 8, respectively) and complete (100% chimerism). In summary, HSC835 dramatically accelerates hematopoietic recovery, abrogating the principal barrier to the successful use of UCB. Such impressive CD34+ expansion may lead to a paradigm shift for both UCB transplantation and banking.

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### More Infections with Transplantation of Bone Marrow, Versus Peripheral-Blood Stem Cells, from Unrelated Donors

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A phase 3 randomized trial of transplantation of bone marrow (BM) versus peripheral-blood (PB) stem cells from unrelated donors showed no significant (sig) differences



**Figure Hematopoietic Recovery**

Panels A and B: Rate of neutrophil and platelet recovery compared to double UCB transplant historical controls. Panels C and D: Comparison of CD34 cell dose and days to neutrophil recovery segregated by SR-1 versus unmanipulated (UMN) unit predominance. Symbols indicate patients transplanted with SR1 plus a companion UMN UCB unit (●) and those with SR-1 UCB as a 'stand alone' graft (▲).

**Figure. Hematopoietic Recovery** Panels A and B: Rate of neutrophil and platelet recovery compared to double UCB transplant historical controls. Panels C and D: Comparison of CD34 cell dose and days to neutrophil recovery segregated by SR-1 versus unmanipulated (UMN) unit predominance. Symbols indicate patients transplanted with SR1 plus a companion UMN UCB unit (●) and those with SR-1 UCB as a 'stand alone' graft (▲).