SESSION G: ALTERNATIVE DONORS; IMMUNE RECONSTITUTION

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Nicord Single Unit Expanded Umbilical Cord Blood Transplantation (UCBT): Final Results of a Multicenter Phase I/ II Trial

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Background: Delayed or failed engraftment after adult UCBT is a major contributor to morbidity, mortality and resource utilization. Increasing the number of hematopoietic stem and progenitor cells within the cord blood graft may overcome this limitation of UCBT. NiCord, developed and manufactured by Gamida Cell, is an ex vivo-expanded, cryopreserved graft derived from an entire cord blood unit (CBU). We conducted a multicenter Phase II study using NiCord as a single stem cell graft.
Methods: The primary endpoint was the cumulative incidence of NiCord-derived neutrophil engraftment. Thirty-five evaluable patients, median age 44 (13-63) were transplanted at 10 sites in the USA, EU, and Singapore. All patients received myeloablative conditioning with a TBI-based (n = 14) or chemotherapy-only (n = 21) regimen. Graft vs. host disease (GvHD) prophylaxis consisted of MMF and tacrolimus or cyclosporine.
Results: NiCord processing resulted in a median 32-fold (20-52 fold) increase in CD34+ cells relative to that reported by the cord blood bank prior to cryopreservation. This translated to a median CD34+ cell dose of 6.3×10^6/kg (1.4-14.9 x 10^6/kg). The cumulative incidence of engraftment at day 42 was 94%. Two patients experienced secondary graft failure; one at day 40 due to HHV6 infection, and another at day 260 due to an overwhelming, lethal adenovirus infection. Neutrophil engraftment occurred at a median of 11 days (95% CI: 9-13 days)(Figure 1). Platelet engraftment occurred at a median 34 days (95% CI:32-42 days)(Figure 2). Full donor whole blood chimerism ([3] 95%) was observed in 100% of engrafted patients by day 100 following transplantation. The incidence of grade II-IV and grade III/IV acute GvHD was 48.6% and 12.2%, respectively. Cumulative incidence of all chronic GvHD was 45%, and moderate/severe cGvHD 11.5% at 1 year following transplantation. The incidence of grade 2-3 bacterial (n = 9) or grade 3 fungal (n = 0) infections was 23.9% by day 100. With a median follow-up of 13 months (range 1-35 months), the 6-month and 2-year non-relapse mortality was 12.8% and 20.3%, respectively. The cumulative incidence of relapse was 27% at 2 years. The Kaplan-Meier estimate of overall survival at 6 months and 2 years was 80.5% and 50.8%, respectively.
Conclusions: The rapid engraftment kinetic coupled with a low graft failure rate and durable hematopoiesis suggests a favorable safety profile of NiCord. Compared to a recently reported multi-center phase II study of adult, unmanipulated myeloablative double UCBT (Barker J, Br. J. Haem 2014), NiCord markedly reduced the median time to neutrophil recovery (11 days vs. 22 days) and platelet recovery (34 days vs. 49 days). UCBT using NiCord has the potential to broaden accessibility to stem cell transplantation and to become a graft of choice for patients without a matched donor. A global randomized phase III study of NiCord vs. standard UCBT is ongoing (NCT02730299).

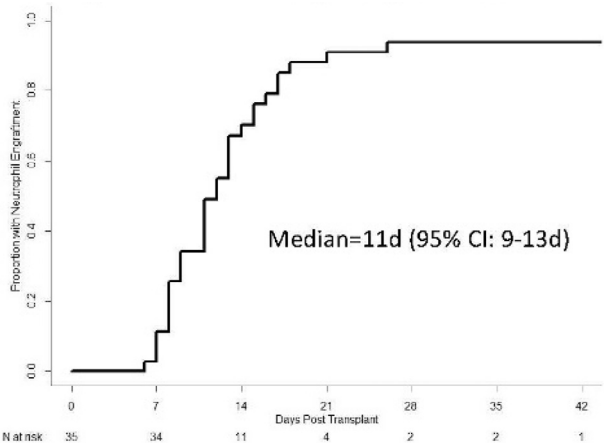

Figure 1. Neutrophil engraftment.

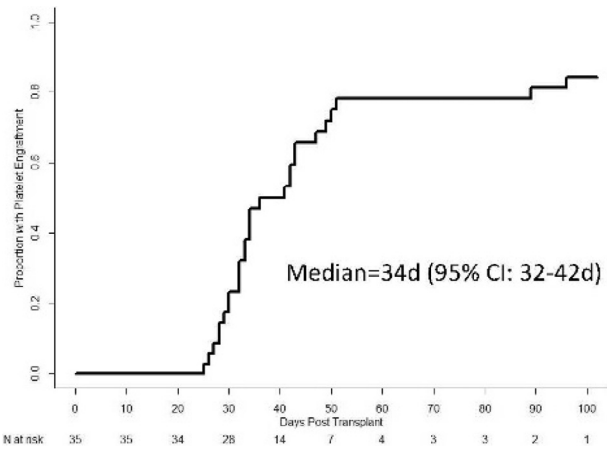

Figure 2. Platelet engraftment.