Oral Presentations

ALLOGENEIC TRANSPLANTS

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PRESERVATION OF PULMONARY DIFFUSING CAPACITY WITH ORAL BECLOMETHASONE DIPROPIONATE: RESULTS FROM TWO RANDOMIZED, PLACEBO-CONTROLLED TRIALS IN ALLOGENEIC GRAFT RECIPIENTS

Chien, J.W., Gooley, T., Sakai, M., Schoch, H.G., McDonald, G.B. Fred Hutchinson Cancer Research Center, Seattle, WA.

Randomized trials show that oral BDP allows rapid tapering of prednisone while controlling gastrointestinal GVHD following allogeneic hematopoietic cell transplant and results in better outcomes (Blood 2007;109:4557–63). In reviewing adverse event data, we noted fewer pulmonary infiltrates in the BDP arm, perhaps because oral BDP is metabolized in the gut to the potent immunosuppressive metabolite 17-beclomethasone monopropionate (17-BMP), some of which is transported via the portal circulation and pulmonary artery directly to the lung. To test the hypothesis that 17-BMP preserved lung function after HCT, we reviewed prospective pulmonary function tests in 120 randomized patients who had been randomized at FHCRC.

Methods: Two studies had randomized patients with GI GVHD to a 10-day induction course of prednisone 1 mg/kg/d for 10 days plus either oral BDP 8 mg/d or placebo. Patients whose symptoms were under control at study day 10 had prednisone tapered rapidly but study drug was continued for 30–50 days. GVHD treatment failures were treated with prednisone 1–2 mg/kg/d. Change in lung function was assessed by comparing pulmonary function tests (PFTs: FEV1, FVC, TLC, DLCO) performed prior to start of conditioning to those obtained post-transplant at day 80, blinded to randomization assignment. **Results:** Sixty patients had been randomized to oral BDP and the same number to placebo. Serial PFTs at day 80 were available from 44 and 50 patients on placebo and BDP, respectively. Significantly fewer patients randomized to BDP (55%) had deterioration of diffusing capacity by transplant day 80, compared to placebo (79%), p = 0.02. No such differences were noted in other PFT parameters. **Conclusions:** These data suggest that oral BDP may have a protective effect on early decline in pulmonary diffusing capacity, which commonly occurs by day 80 after transplant because of interstitial lung injury. We hypothesize that preservation of diffusing capacity was due to delivery of the potent immunosuppressive metabolite 17-BMP to the lungs via GI mucosa, portal vein, and pulmonary artery.

Proportion of patients whose PFTs decreased from pre-HCT baseline to transplant day 80 and magnitude of changes, by randomization assignment (chi square test)

	Baseline to HCT day 80 (# decreased/total #)			Magnitude of % change (mean, range)	
PFT	Placebo	BDP	P	Placebo	BDP
DLCO	32/44 (79%)	27/49 (55%)	.02	−7.95 (−40, +23)	+0.57 (−74, +115)
FVC	24/44 (55%)	25/50 (50%)	.66	−1.85 (−20, +16)	+0.34 (−30, +35)
TLC	25/42 (60%)	29/50 (58%)	.88	−1.67 (−20, +23)	+1.41 (−25, +57)
FEV1	21/44 (48%)	25/50 (50%)	.83	−0.55 (−25, +109)	+1.61 (−27, +34)

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FACTORS AFFECTING 100-DAY AND 1-YEAR MORTALITY FOLLOWING MYELOABLATIVE SINGLE-UNIT CORD BLOOD TRANSPLANTATION IN ADULTS AND ADOLESCENTS: A COMPREHENSIVE META-ANALYSIS OF CIBMTR, NCBP AND EUROCORD

Cohen, Y.C.[1], Scaradavou, A.[2], Stevens, C.E.[2], Rubinstein, P.[2], Gluckman, E.[3], Pacheco, D.[3], Eapen, M.[4], Horowitz, M.M.[4], Shpall, E.J.[5], Laughlin, M.J.[6], Nagler, A.[7], Daniely, Y.[1], Barishev, R.[8], Olmer, L.[8], Freedman, L.S.[8]. [1] Gamida Cell Ltd., Jerusalem, Israel; [2] New York Blood Center, NY, NY; [3] Hospital Saint Louis, Paris, France; [4] Medical College of Wisconsin, Milwaukee, WI; [5] MD Anderson Cancer Center, Houston, TX; [6] Cleveland Cord Blood Center, Cleveland, OH; [7] Sheba Medical Center, Tel Hashomer, Israel; [8] Gertner Institute for Epidemiology and Health Policy Research, Tel Hashomer, Israel.

A retrospective meta-analysis was conducted to examine factors affecting mortality following myeloablative, single-unit cord blood transplantation (CBT) for hematological malignancies in adolescents and adults. Data was collected from three cord-blood transplant registries, Center for International Blood and Marrow Transplant Research (CIBMTR), National Cord Blood Program (NCBP) and Eurocord, and included all records of single, unmanipulated, first myeloablative allogeneic CBT conducted in North America or Europe from 1995 to 2005, with HLA match ≥4/6, in patients with acute leukemia, chronic myeloid leukemia, myelodysplastic syndrome or lymphoma aged 12 to 55, for which 100-day survival data was available. Data was pooled after screening for specified eligibility criteria, creation of common classifications, checking for integrity and consistency, and removal of duplicates. Analysis involved comparison of survival outcomes according to known and exploratory prognostic factors. These covariates were used to build logistic regression models for 100-day and 1-year mortality. Five hundred and fourteen of 742 potential records were found to meet eligibility criteria and were included in the meta-analysis. Overall 100-, 180-day and 1-year mortalities (Kaplan-Meier) were 44%, 56% and 68%, respectively with no significant heterogeneity across registries. Some heterogeneity was observed in the prognostic factors. Multivariate analysis showed cell dose $< 2.5 \times 10^7$/Kg (Odds Ratio 2.74, $p < 0.0001$), disease stage ($p = 0.04$), positive CMV sero-status (OR 1.46 $p = 0.056$), age ($p = 0.002$), female gender (OR 1.45, $p = 0.059$) and transplant center with less CBT experience (contribution of <10 registry records, OR 2.02, $p = 0.0007$) to be associated with higher 100-day mortality; A multivariate model predictive of 1-year mortality included similar covariates: cell dose (OR 1.66, $p = 0.011$), disease stage ($p = 0.03$), CMV (OR 2.25 $p < 0.0001$), age ($p = 0.02$) and center experience (OR 2.25, $p = 0.0002$). Transplant year was not independently predictive of mortality in either of these models. This is the first meta-analysis to pool records from three major CBT registries in the US and Europe. Despite differences in practice patterns, survival data showed remarkable homogeneity. The resulting models will be used in the analysis of the Pivotal Study of StemEx®; transplantation of cord blood expanded *ex vivo* with a copper chelator along with the non-manipulated fraction of the same cord blood unit.

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RISK FACTORS ASSOCIATED WITH GRAFT FAILURE AFTER UMBILICAL CORD BLOOD TRANSPLANTATION (UCBT): A SINGLE CENTER ANALYSIS IN 539 PATIENTS

Doshi, K., Brunstein, C.G., Cao, Q., Wagner, J.E. University of Minnesota, Minneapolis, MN.

UCBT has proved to be a viable alternative for pediatric and adult patients who do not have an HLA matched related or unrelated donor. However, the incidence of graft failure (GF), an often fatal complication, has been reported to be as high as 30% in some series. Therefore, we attempted to identify potential risk factors associated with GF in 539 patients (adult, n = 297; pediatric, n = 242) transplanted with UCB at University of Minnesota between 1994–2006. Patients received one (n = 261) or two (n = 278) UCB units after a myeloablative (MA, n = 338) or reduced intensity (RIC, n = 201) conditioning regimen for malignant (n = 418) or non-malignant (n = 121) disease. GF was defined as evidence of <5%