CIBMTR Best Abstract Awards for Clinical Research

Each year the American Society for Blood and Marrow Transplantation presents Best Abstract Awards to recognize outstanding clinical research. The abstracts receiving the award are those that were scored highest by the Abstract Review Committees. Each award is accompanied by a prize of $1,000. The awards are supported by an unrestricted educational grant from WellPoint, Inc.

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INFUSION OF NON-HLA MATCHED, OFF-THE-SHELF EX VIVO EXPANDED CORD BLOOD PROGENITOR CELLS IN PATIENTS UNDERGOING MYELOABLATIVE CORD BLOOD TRANSPLANTATION IS SAFE AND DECREASES THE TIME TO NEUTROPHIL RECOVERY

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With the goal of overcoming the significant delay in ANC recovery following cord blood transplantation (CBT), we have developed a clinically feasible methodology utilizing Notch ligand for ex vivo generation of increased numbers of CD34+ cells. Having previously demonstrated a significant reduction in ANC recovery time in patients receiving these partially HLA-matched expanded cells in a myeloablative CBT, we are now evaluating whether this product could also support rapid myeloid recovery when used as a non-HLA matched, off-the-shelf product. In this new pilot study, patients undergo single or double ablative CBT plus infusion of progenitors that have been previously expanded from a fresh CB unit and then cryopreserved for future use. To date, 13 patients have been enrolled (see Table for patient/graft characteristics). Importantly, no infusional toxicities have been observed and no serious adverse events have been attributed to the expansion product. All (n = 11) patients have engrafted, with 2 being too early post transplant to evaluate. Median time to achieve an ANC of 100/μl and 500/μl was 11 (range 7 to 20) and 19 days (range 9 to 28), respectively as compared to 19 (range 11 to 37) (p = 0.0001) and 25 days (range 14 to 45) (p = 0.004) in a concurrent cohort of patients receiving ablative double CBT without the expanded cells. Donor(s)/host chimerism studies were performed weekly from day 7 to 28 on peripheral blood flow sorted into myeloid and lymphoid fractions. Similar to our initial expansion trial using partially HLA-matched expanded CB cells, early (day 7) myelomonocytic (CD33 and CD14) recovery is almost entirely (98–100%) due to cells arising from the expansion product. Cells derived from the expansion product are no longer detected at day 14 in all but 2 patients, which is similar to our previous trial in which contribution to donor engraftment in any cell fraction from the expanded unit was no longer detected by day 14 in half of the patients and only two patients had persistence of the expanded cells beyond day 21. Of note, the expanded cells have not been associated with increased incidence or severity of acute GVHD or with development of alloimmunization. All patients are alive; one patient with relapsed disease at the start of conditioning is being treated for post transplant relapse. These promising results warrant evaluation in a randomized phase II study to assess clinical efficacy of this non-HLA matched, off-the-shelf expansion product.

Table. Unit and Patient Characteristics Total Enrolled N = 13

PATIENT CHARACTERISTICS	
Gender, No (%)	
Male	7 (54%)
Female	6 (46%)
Age in years, median (range)	22 (5 to 45)
Weight in kilograms, median (range)	67 (22 to 84)
Diagnosis, No (%)	
ALL	6 (46%)
AML	6 (46%)
MDS	1 (8%)
Follow-up in days, median (range)	180 (16 to 385)
UNIT CHARACTERISTICS	
Number of Unmanipulated Donors, No (%)	
1	2 (15%)
2	11 (85%)
HLA match unmanipulated Donors, No (%)*	
4/6	8 (62%)
5/6	5 (38%)
Infused Cell Doses (pre-freeze)	
Total Unmanipulated TNC/kg x 10^7	6.2 (4.3 to 17)
Total Unmanipulated CD34/kg x 10^6	0.3 (0.09 to 1)
Expanded Product TNC/kg x 10^7	5.8 (2.2 to 10)
Expanded Product CD34/kg x 10^6	6 (3.1 to 11)

*HLA matching reflects the lowest HLA-match of the 2 unmanipulated units.

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CMX001 FOR PREVENTION AND CONTROL OF CMV INFECTION IN CMV-SEROPOSITIVE ALLOGENEIC STEM-CELL TRANSPLANT RECIPIENTS: A PHASE 2 RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, DOSE-ESCALATION TRIAL OF SAFETY, TOLERABILITY AND ANTIVIRAL ACTIVITY

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Introduction: CMX001, an oral Lipid-Antiviral-Conjugate, generates high intracellular levels of cidofovir-diphosphate. CMX001 has potent in vitro activity against dsDNA viruses including herpesviruses, adenoviruses, polyomaviruses, and orthopoxviruses. Patients treated for these infections under individual EIND protocols experienced reductions in virus loads following CMX001 treatment; however, controlled human safety and efficacy data were previously not available.

Methods: This randomized, placebo-controlled, dose-escalation study (CMX001-201) enrolled adult allogeneic CMV-seropositive stem-cell transplant (SCT) recipients from 27 centers in USA. Patients, stratified post-engraftment by acute GVHD requiring systemic glucocorticoid therapy or CMV viremia, were randomized (3:1) to receive CMX001 or placebo into 5 sequential dose-escalating cohorts. Subjects were treated either once weekly (QW) or twice weekly (BIW) for 9 to 11 weeks until Week 13 post-transplant with a 4 to 8 week safety follow-up period. Virology and safety assessments were conducted weekly throughout the treatment period. A DSMB reviewed safety data and directed CMX001 doses for each cohort. Efficacy was measured by a composite endpoint of CMV disease or the appearance/progression of CMV viremia. Patients with these endpoints discontinued study drug and received anti-CMV treatment. This study was registered with ClinicalTrials.gov, NCT00942305.