Annual Sponsor Progress Report

Protocol Title:	Autologous Cell Therapies for Cerebral Palsy-Chronic (ACT for CP)
Date of Report:	January 12, 2015
Reporting Period:	January 1st, 2014 to December 31st, 2014
IND Number:	BB 015246
UT IRB#:	HSC-MS-12-0879
Clinicaltrials.gov Registration #:	NCT01988584

Investigator: Charles S. Cox, Jr., M.D.
The George and Cynthia Mitchell Distinguished Chair in Neurosciences
Director, Children's Program in Regenerative Medicine
Professor, Department of Pediatric Surgery
UTHealth Medical School
6431 Fannin Street, Suite 5.236
Houston, Texas 77030
713.500.7307 (Office)
713.500.7296 (Fax)
charles.s.cox@uth.tmc.edu

Supported by: Cord Blood Registry, Inc.
Let's Cure CP Foundation
Mission Connect, a Program of TIRR Foundation

1. Project Goals and Objectives:

Cerebral palsy (CP) is a major worldwide health problem caused by brain damage during pregnancy, delivery, or in the immediate postnatal period. According to the Centers for Disease Control (2011), Cerebral Palsy is the most common motor disability in childhood, affecting approximately 1 in 303 8-year-old children in the US. It is estimated that the average lifetime costs associated with cerebral palsy are approximately $921,000 per person. There are no effective treatments for CP.

Our stem cell research in neurological disorders, in addition to other research centers, has shown that various types of cell therapies are safe and may enhance recovery from brain injuries such as stroke and TBI. The mechanisms underlying how certain cell therapies exert beneficial effects are likely multi-factorial and include the ability to modulate the inflammatory response after brain injury associated with severe cognitive impairments. Overall, the research data raise the possibility that stem cells may carry therapeutic potential in children chronically disabled with cerebral palsy.

This is a single site, Phase II(a) randomized, blinded, placebo-controlled, cross-over study designed to compare the safety and effectiveness of two autologous stem cell therapies; bone marrow derived mononuclear cells (BMMNCs) versus human umbilical cord blood cells (hUCBs), in children with cerebral palsy (CP). A total of 30 subjects (15/arm) will be enrolled into the study. Subjects will be randomized 2:1 (treatment: sham). All subjects will return for follow-up at 6 months, 12 months, and 24 months post-treatment. At the 12 months post-treatment visit, those subjects who originally received the sham will be offered the BMMNC or hUCB treatment.

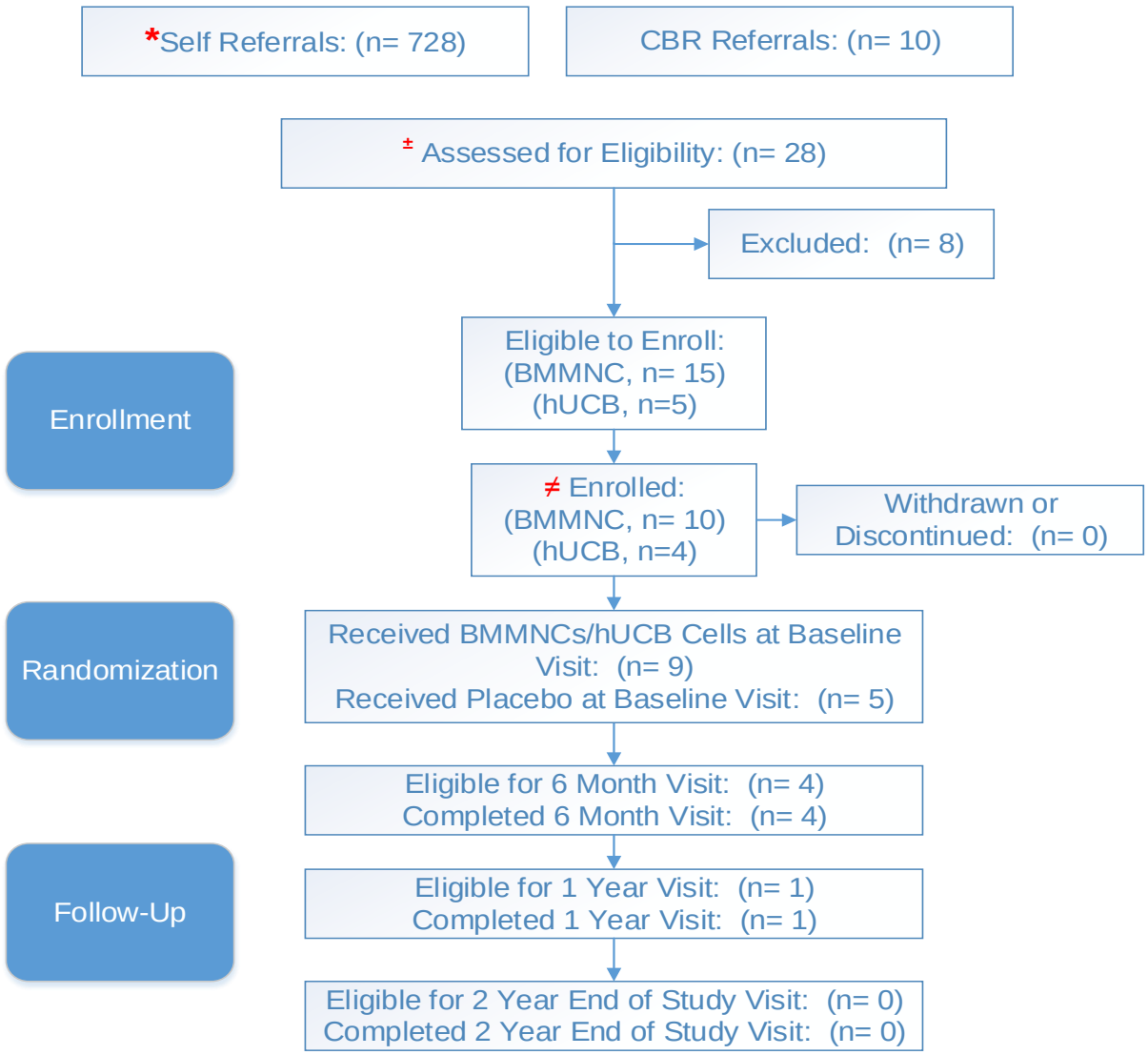
The primary objective of the study is to determine if autologous cells are safe to administer in children with CP. The primary outcome measures are in-hospital toxicity and long-term safety monitoring over the 2-year period of study participation.

The secondary objective is to determine if late functional outcomes are improved following administration of autologous cells when compared to subjects in the control group. Efficacy outcomes will be determined by detailed volumetric analysis of brain MRI's obtained at baseline and the 1 and 2 year visits. Gross motor functions and a battery of psychological assessments will be administered at each study visit and correlated to the brain MRI's.

2. Study Progress:

Subject recruitment and enrollment are presented in Figure A below. The FDA clinicaltrials.gov web site generated the most inquires, and primarily from families without banked umbilical cord blood. Social media (Facebook) sites related to CP also generated a large number of self-referrals. A small number of parents were referred to the study through one of the study sponsors.

Figure A: Screening and Enrollment Diagram



* **Self referral from the Clinicaltrials.gov web site and/or previous contact with the department.**

± **Subjects who appeared eligible following the screening telephone call and submitted medical records and brain MRI images for review.**

≠ **As of the date of this report, six subjects have met eligibility screening and have baseline visits scheduled in the near future.**

Table A: Subject Demographics

Gender:	
Males	7
Females	7
Total:	14

Ethnicity:	
African-American, not of Hispanic origin	0
Native American or Alaskan Native	0
Caucasian, not of Hispanic origin	11
Asian or Pacific Islander	1
Hispanic	1
Other	1
Total	14

The study Medical Safety Monitor reviews real time, blinded subject data summarizing the first 21 days post infusion for infusion-related toxicity and/or adverse events. No adverse events related to the study infusion have been observed.

3. Methodological Problems:

Access to the 3T MRI at MHH has been a limiting factor in scheduling baseline visits. The radiology department is currently under renovation and a second 3T MRI machine will open in the spring of 2015.

We've also had difficulty identifying eligible subjects who have cord blood banked with CBR. CBR will be sending out another informational letter to their clients this month.

We've also networked with the genetic counselors at CBR to increase their awareness of our study and the eligibility requirements.

4. Summary of Results:

Study data will be analyzed after the last subject completes the final study visit.

5. Summary of Preliminary Conclusions:

No information to present at this time.

6. Publications and Presentations:

None at this time.

7. Funds Leveraged into RO1's and other Mission Connect Funding:

None.

8. Study Goals for 2015:

Baseline visits for the bone marrow treatment arm will be completed in the first quarter of 2015. Efforts will be directed to identifying cord blood subjects and completing the follow-up study visits.