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CLINICAL TRIALS — REGENERATIVE MEDICINE

Expanded Access Protocol of Umbilical Cord Blood Infusion for Children with Neurological Conditions: An Update

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ABSTRACT 6

Introduction

An expanded access protocol (EAP) of autologous or sibling umbilical cord blood (CB) infusion was established in 2017 under Investigational New Drug #15949 to provide access to this investigational procedure for individuals with certain neurological conditions who do not qualify for available clinical trials.

Objective

The objective was to report updated enrollment and safety data from a single center EAP of autologous/sibling CB infusion for children with acquired neurological conditions.

Methods

Children with autism, cerebral palsy, and other related conditions were screened remotely under a separate institutional review board-approved screening protocol, including review of parental questionnaires, medical records, basic labs, and CB unit reports. Based on emerging clinical trial data, the minimum cell dose was increased to a total nucleated cell count (TNCC) >2.0 $\times$ 10^7/kg. CB units also had to have viability >70%, negative sterility cultures and maternal donor screening labs, and a segment available for identity confirmation and potency testing, and sibling units had to be at least human leukocyte antigen-haploidentical. CB units were thawed, washed, and infused via peripheral IV after premedication with IV diphenhydramine and methylprednisolone. Some children received repeated doses, when the TNCC allowed.

Results

A total of 2,001 children were screened from November 2017 to June 2021, and 464 children received 494 CB infusions under the EAP, including 20 children who had previously participated in a clinical trial and elected to return to receive a subsequent infusion. Due to COVID restrictions, enrollment was suspended for 18 weeks (March 11, 2020, to July 21, 2020). Patient and CB characteristics are shown in Table 1. Infusions were generally well-tolerated. Forty-one (9%) adverse events, all hypersensitivity reactions, were probably or definitely related to CB infusion. Serious adverse events were documented in 8 children, all expected and unrelated to CB infusion. There were 6 (0.01%) positive post-thaw cultures; none developed infections or required antibiotics. Parental surveys were completed 1 year (n = 244, 72%) and 2 years (n = 105, 51%) post-infusion. Parental assessment varied regarding clinical improvement.

Discussion

Autologous/sibling CB infusions conducted under an EAP for children with neurological conditions are safe and feasible with varied reported responses to the infusions. CB eligibility was amended to incorporate early phase clinical trial outcomes regarding cell dose. Efficacy continues to be evaluated in ongoing clinical trials.

Table 1 Recipient, cord blood, and infusion characteristics

Characteristics	Median	Range or %
Patient characteristics (*N* = 464)		
Age, years, median (range)	6.0	0.2-23.4
Sex, *n* (%)		
Male	335	72%
Female	129	28%
Race, *n* (%)		
Caucasian	335	72%
Non-Caucasian	129	28%
Diagnosis, *n* (%)		
Autism	278	60%
Cerebral palsy	122	26%
Other	64	14%
Number of infusions, *n* (%)		
1	419	90%
2+	45	10%
Cord blood infusion characteristics (*n* = 494)		
Source, *n* (%)		
Autologous	246	50%
Sibling	248	50%
Precryo TNCC ($\times 10^8$), median (range)	4.34	0.3-22.4
Precryo viability (%), median (range)	94	74-100
Post-thaw cell dose infused ($\times 10^7$/kg), median (range)	2.50	0.07-90.2
Positive post-thaw sterility. *n* (organisms)	6	Coagulase negative *Staphylococcus*, ×5 *E. coli*, ×1