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

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ABSTRACT 31

Introduction

Intravenous infusion of banked autologous and sibling umbilical cord blood (CB) is being studied in children with acquired neurological conditions and has demonstrated safety and feasibility in phase I/II studies. To provide access to this investigational procedure while efficacy trials are conducted, an expanded access program (EAP) was developed.

Objective

The aim is to report early outcomes of a single center EAP enabling infusion of autologous/sibling CB for children with acquired neurological conditions.

Methods

A protocol for CB infusion utilizing established standard operating procedures was filed under Investigational New Drug #15949. Potentially eligible children with autism, cerebral palsy, and related conditions were screened remotely under a screening protocol via parental questionnaires, medical records, and labs. Children with genetic syndromes, immunodeficiencies, or medical fragility were ineligible. Autologous/sibling CB units (CBUs) were qualified to ensure a pre-cyropreservation total nucleated cell count (TNCC) $>1 \times 10^7$/kg, viability >70%, negative sterility cultures, and negative maternal donor screening tests. Sibling pairs had to be at least haploidentical by human leukocyte antigen. A segment of each CBU was tested for viability, potency, and identity confirmation. On the day of infusion, recipients were premedicated with intravenous diphenhydramine and methylprednisolone. The CBU was thawed, washed, and infused over 10 minutes via peripheral IV. When the TNCC permitted, CBUs could be divided for repeated doses.

Results

More than 1,400 children have enrolled in the screening protocol to date. From November 2017 to June 2019, 276 children received 302 CB infusions under the EAP. Table 1 shows recipient and CB characteristics. Median pre-cryopreservation TNCC of CBUs was 7.8×10^8, and median infused dose was 2.5×10^7/kg. Infusions were well tolerated. The only related adverse events were transient infusion reactions, which occurred with 3.9% of infusions (n = 12, one serious adverse event). Despite negative sterility cultures pre-cryopreservation, there were 6 (2%) positive cultures post-thaw. No child required treatment or developed an infection post-infusion. One-year follow-up questionnaires were completed by 54 of 83 (65%) families. Parental assessment of clinical improvements varied.

Discussion

An EAP including procedures for remote screening of patients and CBUs was developed to provide access to autologous/sibling CB infusion for children with acquired neurological conditions. In general, CB infusions have been safe and feasible, with variability in parent-reported outcomes. Standard phase II/III clinical trials will be required to evaluate efficacy.

Table 1. Recipient, cord blood, and infusion characteristics

Patient characteristics (*n* = 276)	Median	Range or Percentage
Age, years, median (range)	5.8	0.2–18
Sex, *n* (%)		
Male	194	70%
Female	82	30%
Race, *n* (%)		
Caucasian	186	67%
Non-Caucasian	90	33%
Diagnosis, *n* (%)		
Autism	160	58%
Cerebral palsy	70	25%
Other	46	17%
Number of infusions, *n* (%)		
1	253	92%
2+	23	8%
Cord blood (*n* = 277) and infusion (*n* = 302) characteristics		
Source, *n* (%)		
Autologous	160	58%
Sibling	117	42%
Precryo TNCC ($\times 10^8$), median (range)	7.8	0.4–79.5
Precryo viability (%), median (range)	95	74–100
Post-thaw cell dose infused ($\times 10^7$/kg), median (range)	2.5	0.1–43.3
Positive post-thaw sterility, *n* (organisms)	6	Coagulase negative staphylococcus ×5 *E. coli* ×1

Post-thaw $CD34^+$ dose infused will be reported. Abbreviations: Precryo, pre-cryopreservation; TNCC, total nucleated cell count.