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Reply

To the Editor:

We appreciate the questions raised by Thanh et al about our clinical trial evaluating the safety and efficacy of intravenous umbilical cord blood infusion for the treatment of children with autism spectrum disorder (ASD). We did not target CD34 dosing in this clinical trial because our preclinical studies and early-phase clinical trial data in children with ASD and children with cerebral palsy (CP) did not show any association between improvement and CD34 dosing.

Our data showed that the cell responsible for modulation of neuroinflammation, stimulation of oligodendrocyte proliferation, remyelination, and increasing whole brain connectivity is the CD14+ monocyte in cord blood.[1-4] Cord blood banks do not measure CD14 cell content but do measure total nucleated cells (TNCCs) and CD34. For this reason, selection of cord blood units for the participants with ASD and CP in our clinical trials has been based on TNCC. We are investigating whether infused CD14 cell doses correlate with response but do not have that data at this time.

In our first randomized trial using autologous cord blood in young children with CP, we reported an effective dose threshold of 25 million cells/kg.[5] We saw the same trend in our initial phase I trial in children with ASD.[6] Since that time, we have targeted greater TNCC doses in our trials involving children with CP and have observed a dose effect up to 100 million cells/kg (unpublished data). For our trials with children with ASD, we target a minimal dose of 25 million cells/kg. Although CD34 cell dosing is quantitated in all our trials, we have not seen any relationship between CD34 dose and response. The CD34 doses in the trial reported in *The Journal* are typical of CD34 doses achievable with an unmodified cord blood transplant or cord blood infusion. We are following children in the trial published in *The Journal* for a period of 12 months postinfusion and will be reporting the 12-month outcome data at a later date.

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Supported by The Marcus Foundation, Atlanta, GA. G.D. reports technology unrelated to the submitted work that has been licensed and she and Duke University School of Medicine have benefited financially. G.D. has patents 62757234, 62757226, 15141391, and 62470431 pending. J.K. has a patent 62470431 pending and Duke University School of Medicine signed an option agreement with CryoCell International to license the clinical indication in this study.

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Premature congenital heart disease: building a comprehensive database to evaluate risks and guide intervention

To the Editor:

We read with interest the report by Matthiesen et al.[1] This large population based study found a 2-fold increase in incidence of preterm birth in the setting of major congenital heart disease (CHD) and delineated specific subgroups of CHD with even higher adjusted risks (specifically, right ventricular outflow tract obstructions). This study fills a major gap of knowledge with respect to understanding the link between certain CHD lesions and the insults to the fetal environment, and highlights that little is known about the impact of perinatal risk factors on outcomes for this vulnerable preterm population. This is in part due to the recognition that no existing neonatal or cardiac focused database adequately collects the full spectrum of data points (eg, prenatal, perinatal, postnatal, and surgical) critical to perform outcomes research and identify best practices for the neonatal population with CHD. In addition, unique to preterm patients with CHD, postnatal