

Title: Trial of Late Surfactant to Prevent BPD – A Study in Ventilated Preterm Neonates Receiving Inhaled Nitric Oxide: The TOLSURF Study

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Synopsis:

The hypothesis is that late doses of surfactant, in addition to iNO, administered to Extremely Low Gestational Age Newborn (ELGAN) infants <28 weeks gestation who continue to require mechanical ventilation between 7 and 14 days of age will increase survival without BPD. Further, that there will be no adverse effects of surfactant treatment on short- or long-term outcomes. The aims are to (i) Assess the effect of late doses of surfactant in ventilated ELGANS receiving inhaled nitric oxide on survival without BPD and (ii) Assess effects of late surfactant treatment on surfactant status and lung inflammatory biomarkers, and establish a DNA repository for genomic studies of the pathogenesis of BPD.

Infants born prematurely are at risk for both respiratory distress syndrome (RDS) and bronchopulmonary dysplasia (BPD), defined as a continuing requirement for ventilatory support and/or supplemental oxygen at 36 weeks postmenstrual age (PMA). BPD affects more than 70% of infants of < 30 weeks gestation who require ventilatory support after 7 days of age. Severe forms of BPD are associated with long-term pulmonary disability, neurodevelopmental abnormalities and death. It is estimated that there are up to 15,000 new cases of BPD annually in the United States.

Most very premature newborn infants are deficient in pulmonary surfactant at birth, and current clinical care includes surfactant replacement therapy to reduce the incidence and severity of RDS. Despite surfactant treatment at birth, premature infants often need mechanical ventilatory support and/or supplemental oxygen during the first week of life and many have a continuing requirement for respiratory support after the first week, often requiring reintubation or increased ventilatory support. We found that most of these infants experienced respiratory deteriorations that were associated with dysfunctional surfactant and low content of surfactant proteins (SP) B and C. Although inhaled nitric oxide (iNO) started between 7 and 14 days of age significantly improves outcome in this group of infants, these infants still have episodes of surfactant dysfunction.

We propose that episodes of surfactant dysfunction in chronically ventilated infants contribute to development of BPD by increasing lung inflammation and injury secondary to greater exposure to oxygen and volutrauma, and by restricting distribution of iNO secondary to atelectasis. Based on these observations, we propose to conduct a multi-center, randomized, controlled trial of surfactant treatment for 575 infants ≤ 30 weeks gestation receiving iNO for lung disease requiring mechanical ventilation beyond 7 days of age.