SUMMARY
Study Registry for Severe Retinopathy and Treatment on Visual Outcomes of Premature Neonates

Sponsor
MEDNAX Center for Research, Education and Quality

Steering Committee
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Study type – Prospective Descriptive study
Multicenter study - Number of sites – 30
Study enrollment goal - 600
Site enrollment goal – 20

Purpose
The purpose of this study is to determine what factors influence the visual outcomes of infants with severe retinopathy of prematurity (ROP) and to monitor the outcomes

Background
With the improved survival of very low birth weight (VLBW) infants during the past decade, ROP continues to be a source of significant morbidity. Wide intercenter variability exists in the incidence of severe ROP (stage 3, 4). Quality improvement efforts have reduced the occurrence of ROP but have not eliminated this morbidity which is a common cause for blindness in children. Infants with significant ROP are at increased risk for visual impairment and blindness.(1-4)

Recent studies have generated significant concern about the best way to prevent ROP; and if it does develop how best to treat severe ROP.(5-8) Using lower oxygen saturation is associated with a decrease in severe retinopathy among survivors, but it may also be associated with an increase in mortality.(5,6) Treatment strategies are also in a state of evolution once severe ROP has developed. Mintz-Hittner and colleagues found that intravitreal bevacizumab monotherapy, as compared with conventional laser therapy, in infants with stage 3+ retinopathy of prematurity showed a significant benefit for zone I but not zone II disease. Development of peripheral retinal vessels continued after treatment with intravitreal bevacizumab, but conventional laser therapy led to permanent destruction of the peripheral retina.(8) This trial was too small to assess safety.

The safety of therapy for retinopathy of prematurity involves not only the eye but also potentially systemic issues.(9) Intravitreal bevacizumab reaches the systemic circulation and this raises the concern of untoward effects on the infant’s developing organs. However, such an effect has not been documented. The dose of intravitreal bevacizumab is a fraction of the dose used for cancer treatment, and the amount of circulating bevacizumab is very small. Breakdown of the blood–retina barrier could result in an increase in the level of drug in the circulation, but probably not an appreciable increase. To determine systemic safety with statistical assurance would require a huge sample size. No such trial is currently planned. Reynolds suggest that continued vigilance will be important as use of the drug increases based on the results of recent clinical trials.(9)
Phase 4 surveillance of drug use, evaluation of the influence of drugs on outcome (pharmacovigilance) and comparative effectiveness research are important. Safety surveillance is designed to detect any rare or long-term adverse effects over a much larger patient population and a longer time period than was possible during the Phase I-III clinical trials. It is not our intent to influence clinical care of these patients but instead to monitor the influence of the prescribed care on outcomes.

**Study Population**

**Inclusion Criteria**
1. Documentation of informed consent. Parent must provide contact information to obtain follow-up data on their child
2. Inborn and those admitted within 7 days of birth
3. Infant with a diagnosis of stage two (2) ROP or higher
4. Site ability to plan close ophthalmological follow-up data due to significant and persistent ROP
5. Parents must agree to report outcomes following each ophthalmology visit and overall outcomes for up to five (5) years of age
6. Ability to obtain follow-up data on outcomes if the child is transferred to another facility
7. No known major congenital anomalies

**Exclusion Criteria**
1. ROP stage one (1) or less
2. Parents unwilling to participate in follow-up
3. Major congenital anomalies as outlined in the protocol

**Outcome Measures**
1. Identification of visual acuity in neonates who were treated for ROP
2. Neonates who develop blindness
3. Ocular outcomes we will report and consider secondary adverse outcomes:
   - Recurrence of stage 3+ retinopathy of prematurity in one or both eyes in zone I or posterior zone II
   - Recurrence of neovascularization in one or both eyes arising from the retinal vessels and requiring retreatment
   - Macular dragging
   - Retinal detachment peripheral
   - Retinal detachment complete
   - Cornea opacity requiring corneal transplant
   - Lens opacity requiring cataract removal
   - Vitrectomy
   - Vitreous hemorrhage
   - Significant refractive errors
   - Strabismus
   - Glaucoma
   - Astigmatism
   - Amblyopia
   - Myopia
Follow-up
Follow-up will be completed on all enrolled subjects. Those subjects who have completed ophthalmologic examination and have no visual impairment or disorder will complete follow-up for one year post study enrollment. Follow-up will be completed every three months through phone calls to the parents and/or the ophthalmologist or retinologist. Those subjects who are identified with a visual impairment or disorder will complete follow-up for five years post study enrollment. The first year will consist of follow-up phone calls every three months to the parents and/or ophthalmologist or retinologist, then every six months for years two through five.

References


