

Bronchiolitis (BRO) Overview



- Common lower respiratory tract infection and leading cause of infant hospitalization
- Significant impact on the elderly with >220k hospitalizations per year in the US
- No drugs approved for the treatment of BRO patients
- Standard of care in the hospital is oxygen and hydration

Market Dynamics: Bronchiolitis (BRO)



150k infant hospitalizations per year in the US for bronchiolitis*

180K elderly hospitalizations per year in the US due to RSV** implying more than 220k for bronchiolitis

AIT price will be based on reduced length of hospital stay from trials

Total US market size in excess of \$2 billion

Anticipate ex-US market to be comparable to the US market

There is no competition

*Pelletier et al. Direct medical costs of hospitalizations in the United States, Pediatrics 2006

**Falsey et al. Respiratory Syncytial Virus infection in elderly and high risk adults, NEJM 2005

Trial Design

- Randomized, Prospective, Double-blind
- 43 patients (age: 2-12 months) with bronchiolitis (mostly due to RSV)
- N=21: 160 ppm NO + O₂ 5x/day for 30 minutes up to 5 days
- N=22: Supportive Care (O₂ & hydration)
- 3 follow up visits at 2, 3 & 4 weeks post discharge

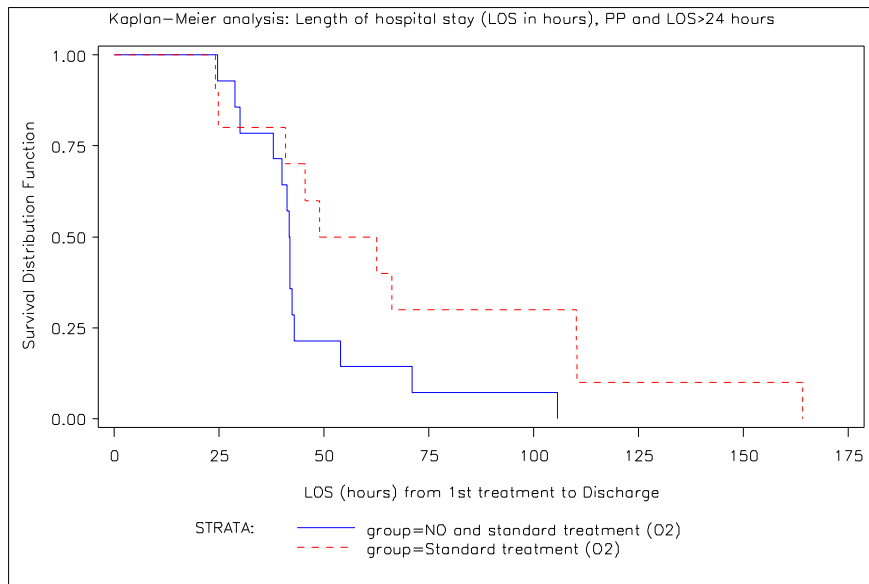
Trial Highlights

- Single center at Soroka University Medical Center in Israel
- Presented at ATS 2015 in an oral session
- No treatment related SAEs
- Reduced length of hospital stay by >24hrs
- Statistical significance achieved in proposed phase III primary endpoint (Clinical Composite endpoint)

Publication Pending

Decrease in Hospitalization time

(Per Protocol, N=24, minimum of one day of hospitalization)



P-value 0.0587

~34% reduction in time of hospitalization, a validated end point

On average patients stayed one day (24 hours) less in the hospital with Nitric Oxide treatment compare to standard treatment

Randomized, Double Blind Trial

- Enroll 94 subjects at 3+ sites in Israel with a 1:1 randomization between 160 ppm NO + supportive care (O₂ + hydration) and supportive care alone
- Subjects will be 0-12 months old with acute bronchiolitis requiring hospitalization with at least 28 weeks of gestation
- PE (primary endpoint): the difference in hospital length of stay (discharge time based on physician decision)
- SE (secondary endpoint): the difference in time to clinical improvement based on the Modified Tal score (score ≥ 8 and ≤ 10 to enroll, ≤ 5 is goal)
- SE: the difference in time to S_pO₂ of $\geq 92\%$
- SE: Safety (specifically methaemoglobinemia and NO₂ levels) and Tolerability
- Treatment will be five 30 minute sessions per day not to exceed 25 treatments

Key Changes v. Phase 2

- Age was 2-12 months
- Gestation was a minimum of 36 weeks
- Tal score to enroll was ≥ 6 and ≤ 10
- ITT analysis was not restricted to hospitalized subjects
- Length of Stay was based upon hospital discharge, not physician decision
- Analysis included 24 subjects