Hospira

2.0 SYNOPSIS

Name of Sponsor: Hospira,Inc.
Name of Finished Product: Precedex™ [Dexmedetomidine Hydrochloride (HCl) Injection]
Name of Active Ingredient: Dexmedetomidine HCl
Title of Study: A Phase II/III, Open-Label, Multicenter, Safety, and Efficacy Study of Dexmedetomidine in Preterm Subjects Ages ≥ 28 Weeks to < 36 Weeks Gestational Age
Investigators and Study Center(s): This was a multicenter trial conducted at 4 investigator sites. Only 3 sites enrolled the study subjects. The list of the Investigators with the study centers is available in the appendices.
Publication (reference): Not applicable
Study Period: 19 Mar 2012 to 30 May 2012
Phase of Development: II/III
Objectives: The primary objective of this study was to characterize the safety and efficacy of Dexmedetomidine (DEX) administered as an intravenous (IV) loading dose followed by a continuous IV infusion in preterm subjects, ages ≥ 28 weeks through < 36 weeks gestational age.
Methodology: This was a Phase II/III open-label, multicenter, safety, and efficacy study of DEX in preterm subjects. All subjects received the DEX 0.2 mcg/kg over 10 or 20 minutes as loading dose followed by DEX continuous maintenance infusion at the rate of 0.2 mcg/kg/hr for a minimum of 6 hours and up to 24 hours. Efficacy evaluations were conducted by assessing the level of sedation using the Neonatal Pain, Agitation, and Sedation Scale (N-PASS), developed to assess sedation and pain/agitation in neonates.
Number of Subjects: A total of 6 subjects were enrolled in to the study as per the plan. All the subjects qualified to be included in the safety evaluable and efficacy evaluable population.
Diagnosis and Main Criteria for Eligibility: Initially intubated and mechanically ventilated preterm subjects ≥ 28 weeks through < 36 weeks, gestational age, having a weight of > 1000 g, in an intensive care setting anticipated to require at least 6 hours of continuous intravenous sedation.
Test Product, Dose and Mode of Administration, Batch Number: DEX is to be administered as a 2-stage infusion: A 10- or 20- minute loading dose infusion of 0.2 mcg/kg of DEX followed by a continuous fixed maintenance dose infusion of 0.2 mcg/kg/hr of DEX for at least 6 hours and up to 24 hours post-operatively. The dose of DEX could be diluted in 0.9% sodium chloride or dextrose 5% (D5W) to one of the following concentrations- 4 mcg/mL solution; 2 mcg/mL solution; 1 mcg/mL solution or 0.5 mcg/mL solution. Only one batch of the DEX was used in this study and the batch number was 95-261-DK.

Duration of Treatment: Each subject received a 10- or 20- minute loading dose infusion of DEX followed by a continuous fixed maintenance dose infusion of DEX for at least 6 hours but not more than 24 hours.

Reference Therapy, Dose and Mode of Administration, Batch Number: Not applicable

Criteria for Evaluation:

Efficacy:

Primary Efficacy Endpoint

The primary efficacy endpoint for the study was the frequency of subjects requiring any use of rescue medication, midazolam (MDZ), for sedation during DEX infusion.

Secondary Efficacy Endpoints

- Incidence of rescue medication use (fentanyl or morphine) for analgesia during DEX infusion
- Amount of rescue medication (MDZ) for sedation during DEX infusion
- Amount of rescue medication for analgesia during DEX infusion
- Change from baseline in vital signs (heart rate, blood pressure, mean arterial pressure), respiratory rate and oxygen saturation measures during DEX infusion
- Time spent with a total N-PASS score >3 during DEX infusion
- Time to extubation was explored in DEX-exposed subjects

Safety:

- the incidence of AEs
- Changes from baseline in vital signs
- Changes from screening in clinical laboratory tests
- Changes in input/output fluid balance
- Changes from baseline in ECG
- Use of rescue regimens to support vital signs
- Use of adjunct medications

Statistical Methods: The statistical analyses were performed using SAS, version 9.1. All statistical tests were 2-sided and p-values ≤ 0.050, after rounding to 3 decimal places, were considered statistically significant unless otherwise specified. Descriptive statistics were used.

SUMMARY – CONCLUSIONS

EFFICACY RESULTS:

No subjects received rescue midazolam for sedation during study drug infusion. One subject received fentanyl (1mcg/kg) as rescue medication for analgesia during study infusion. Only 2 out of the 6 subjects had N-PASS score > 3 during DEX infusion. Subjects spent a short period of time with a total N-PASS score > 3 indicating most subjects were adequately sedated and not manifesting signs of pain/agitation. The median time for successful extubation was 37.3 hours.

SAFETY RESULTS:

Three subjects experienced a total of 5 AEs during the study, of which 3 were treatment emergent adverse events (TEAE). None of the AEs were severe in intensity. None of the AEs were considered related to the study drug. There were no SAEs reported during the study. There were no treatment-emergent SAEs

leading to death, no other treatment-emergent SAEs, and no TEAEs that led to DEX discontinuation.

CONCLUSION: Overall conclusions are as follows:

- Dexmedetomidine at 0.2 mcg/kg loading dose and 0.2 mcg/kg/hr maintenance dose was effective at sedating initially intubated and mechanically ventilated premature infants, ≥ 28 weeks to < 36 weeks gestational age. No subject received rescue MDZ for sedation during DEX infusion.
- Most premature neonates (5 out of 6) did not require additional medication for pain while on DEX infusion. One subject received rescue medication for analgesia during the study infusion.
- Subjects spent a short period of time with a total N-PASS score > 3 indicating most subjects were adequately sedated and not manifesting signs of pain/agitation.
- Dexmedetomidine was safe and well tolerated in initially intubated and mechanically ventilated premature infants, ≥ 28 weeks to < 36 weeks gestation age. There were no deaths, SAEs, TEAEs leading to DEX discontinuation or dose-limiting toxicities that led to DEX discontinuation.
- In general, changes from baseline were not clinically significant for laboratory parameters, vital signs, physical examination, or ECGs.

Date of the report: 07 Aug 2012